DEATH HATH MANY A DOOR

Being an Analysis of the causes of death of 250 infants under the age of two years

A Thesis submitted by

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CERTIFICATE

I hereby declare and affirm that this Thesis is entirely my own work and composition.

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CHAPTER 6 PREVENTION OF MORTALITY AND MORBIDITY IN INFANCY

SUMMARY

A review of the causes of death of 250 infants under the age of two years paves the way for a discussion on the present position as regards prevention of mortality amd morbidity in infancy and possible future advances in this field.

The Introduction outlines the circumstances in which this study took place and divides the deaths into three groups, death in the neonatal period, death in the post-neonatal period following a period of serious, recognised illness and death in the post-neonatal period occurring either suddenly or unexpectedly.

Chapter 1 analyses 103 neonatal deaths, discussing the morbid anatomical and histological findings at autopsy, the clinical picture and the correlation of the clinical and pathological findings. The main groups, birth trauma, frank infective processes, congenital disease, erythroblastosis foetalis, trauma other than birth injury, neonatal asphyxia and the respiratory distress syndrome are outlined.

Chapter 2 discusses the cause of death in 64 infants who died after the 14th day of life following a history of illness of more than six hours duration. Post-mortem findings and clinical data are presented in a series of cases illustrating gastro-enteritis, pneumonia, other infective conditions, congenital defects and accidental deaths.

Chapter 3 analyses the clinical and morbid anatomical findings in 83 cases of sudden or unexpected death in infants with histological, bacteriological and biochemical data in a proportion. This series includes 15 cases with a brief acute history of a few hours as the shortness of the illness led to unexpected death. Seven cases were due to accidental death, the remaining 76 are discussed from the clinico-pathological aspects, with illustrative microphotographs. General conclusions as to the mechanism of these deaths, based on this personal

series, are presented.

A discussion on sudden or unexpected death in infancy follows in Chapter 4. The literature on the subject is reviewed and correlated with the findings reported in the previous chapter; it is concluded that sudden or unexpected death in infancy can be divided into two main groups, those with a well-defined cause of death such as trauma, major congenital abnormalities, frank meningitis and the like and those in which autopsy reveals an asphyxial picture only. The histological and clinical features in these latter cases are discussed and it is concluded that where an unequivocal macroscopic cause of death is not found, the great majority of sudden or unexpected deaths in infancy are due to acute infective conditions, septicaemic or pulmonary, bacterial or virological.

Chapter 5 discusses infant mortality in general. The pattern of infant mortality since 1900 is illustrated from the annual reports of the Registrar General and the main causes of death in infancy are discussed by reference to the literature and the findings in Chapters 1, 2 and 3. These main causes are the respiratory distress syndrome, congenital malformations, erythroblastosis foetalis, and infections in infancy, particularly of the respiratory and gastro-intestinal tracts.

The final chapter is devoted to consideration of the prevention of mortality and morbidity in infancy. The factors involving the potential mother, the father, the pregnant woman and her conceptus, delivery and the neonate and the infant which may lead to disease or death are discussed in relation to preventive paediatrics. It is concluded that high standards of professional care, continued research, extension of community health programmes and education of the population in health measures can continue to improve the impressive fall in infant mortality and morbidity which has taken place during this century.

INTRODUCTION

"Death hath so many doors to let out life."

Beaumont and Fletcher

During the period when the author was holding the appointment of Senior Pathologist with the British Army of the Rhine, post-mortem examinations were carried out on 250 infants, the children of British or Canadian service personnel, who died under the age of two years. This figure relates only to those who were born alive; it represents practically all the actual deaths as requests and permission for post-mortem examination were made and given in nearly every case.

The examinations were carried out at mortuaries in connection with seven military hospitals, they were reported to and discussed with me before the autopsy, a number were performed personally and where histological examination was carried out, this was done or reviewed by me in all cases.

The clinical histories and post-mortem findings, including histological examination in a number, and bacteriological or biochemical investigation in a small proportion, form the material on which this thesis is based. To a certain extent the study is in retrospect, as it was only a year or two after my assuming the appointment that particular interest in death in infancy, especially sudden or unexpected death, was aroused personally and a start made on the collection of the material. Hence it is that full studies, including histological examination, are not always complete, particularly in the earlier years. But this position holds for most studies which are based on routine practice and not on purely research projects.

The aim of the study is threefold. While we have come far from the statement by Farr (1864) over one century ago that "The children of the idolatrous tribes who passed them through the fire to Moloch scarcely incurred more danger than is incurred by the children born in several districts of our large cities," there can be as yet no complacency as

regards infant mortality figures. Much of the fall in infant mortality during the past century has been due to increasing appreciation of the cause of such mortality and hence awareness of possible causes of prevention. There is, however, still an appreciable infant mortality and the first aim of this investigation was to add a further series to published studies of the causes of death in infancy and to discuss lines along which improvement could be made.

As "death hath so many doors," an analysis of cases of this nature reveals a wide range of pathological conditions and a review of these is academically stimulating. This was the second aim.

At a meeting of the Medico - Chirurgical Society of Edinburgh on 1st July, 1892, Templeman read a paper on suffocation of infants in Dundee during the period 1882 - 1891. All were ascribed to mechanical suffocation. Since then, this interpretation of sudden or unexpected death in infancy has been largely abandoned. The third aim of the study was to examine cases of this nature in the series under review, to consult pertinent literature on the subject and to see how far this problem has been resolved.

No rigid classification of causes of death in series of this nature is possible as many cases, in particular asphyxial deaths in the new-born, are associated with multiple factors, both clinical and pathological. In this study, deaths fell into three main groups:-

1. Death in the neonatal period, for the purpose of this review taken as the first fourteen days of life.
2. Death in the post-neonatal period (i.e., after the fourteenth day of life) following a period of serious, recognised illness, and
3. Death in the post-neonatal period occurring either suddenly or unexpectedly, an illness of six hours or less being taken as the dividing line between this group and those who were

recognised to be seriously ill with a grave prognosis.

Preliminary classification of the 250 cases along these lines shows:

Neonatal deaths	103 (41.2%)
Death after serious illness	64 (25.6%)
Sudden or unexpected deaths	83 (33.2%)

Chapters 1 - 3 deal with an analysis of the cases in these three groups, a discussion follows in Chapter 4 and 5 and Chapter 6 is devoted to a review of the present position as regards prevention of these conditions and possible future advances.

CHAPTER 1

NEONATAL MORTALITY

"A little soul scarce fledged for earth,
Takes wing with heaven again for goal,
Even while we hailed as fresh from birth,
A little soul."

Swinburne (1837-1909)

PREAMBLE

The first essential in a consideration of deaths in the neonatal period is to have a meaningful classification, that is one which will aid in the quest for the factors underlying the cause and hence point to possible means of prevention. Such classification, however, is not easy. It has been shown many times in the past, and the present study will bear this out, that much the same morbid anatomical picture is found in a wide range of causes of death, involving a number of maternal, obstetrical or foetal factors, so that a purely pathological approach is of little value. A clinical approach, however, has similar drawbacks as in any one case, for example, maternal toxaemia, prematurity of the infant and a difficult forceps delivery may all contribute to the cause of death, but which factor has to be implicated primarily? This difficulty in classification is reflected in the diverse methods used by various authors. A few series follow as examples:

In the Medical Research Committee (now Council) Special Report Series of 1917, Brend classified infant mortality in relation to the pathological cause into:

Respiratory

Epidemic diarrhoea and enteritis

Developmental disease and malformations (comprising premature births, congenital deformities, atrophy (sic), debility and marasmus) and

Other diseases.

Bound et al (1956) classfied the causes of neonatal death as

Intra - uterine asphyxia

Congenital malformations

Birth trauma

Pulmonary syndrome of the new-born

Pneumonia

Erythroblastosis

Intraventricular haemorrhage

Miscellaneous and

Previability

The Bulletin of the Ministry of Health (Brook, 1961) used a more clinical approach, classifying neonatal death by first cause as:

Complications of pregnancy

Delivery with specified complications

Congenital malformations

Birth injury

Asphyxia and infection of the new-born and

Other diseases peculiar to infancy, etc; according to the International Code of Diseases

Butler and Bonham (1963), in a comprehensive series of statistical tables relating to factors involved in perinatal mortality (including still-births), analysed the causes of death by post-mortem findings and classified them into no less than 17 groups, but there was considerable overlap between these (for example, in 42% of cases of intraventricular haemorrhage (Cause 11), hyaline membrane (Cause 9) was present).

These examples, many more could be cited, show that comparison between series is difficult, they make assessment of possible worth-while preventive measures more difficult as stress is placed on different aspects

in the different series, and they indicate that knowledge is still far from complete.

It is proposed to examine the 103 cases of neonatal death in this series from the pathological and clinical findings with a view to arriving at a simple classification. Important conditions will be discussed in Chapter 5.

As a preliminary, the series can be divided into 48 (46.6%) premature infants, the birth weight being less than 5lbs 8ozs, and 55 (53.4%) non-premature infants. Brief clinical, morbid anatomical and histological notes on these 103 neonatal deaths have been tabulated as Appendix A. Analysis of the obstetrical histories shows that in 20 of the premature infants and in 19 of the non-premature babies there was no indication of any significant maternal ill-health, labour was uneventful by via naturales and the infant at birth had no clinical evidence of any significant disease.

PART 1 - THE PATHOLOGICAL PICTURE

A. MORBID ANATOMY

In 46 out of the 103 neonatal deaths, post-mortem examination enabled the cause of death to be stated unequivocally as due to a well-defined pathological process, viz:

	Premature	Non-premature	Total
Birth Trauma	6	7	13
Infection Pneumonia	2	6	8
Septicaemia	1	-	1
Hepatitis	-	1	1
Congenital deformity or disease	3	15	18
Erythroblastosis neonatorum	2	2	4
Trauma (Road traffic accident)	-	1	1
Totals	14	32	46

In the remaining 57 cases, comprising 34 premature and 23 non-premature infants, the cause of death was not so precise. The external appearance in a number of cases showed cyanosis of the face and extremities, this was not universal and there was no appreciable difference in the incidence of this compared with the cases showing a definite pathological cause of death.

The central nervous system showed appreciable congestion in about half the cases compared with all cases of cerebral birth trauma and most of the cases of infection; meningeal petechial haemorrhages were observed in only one case and intraventricular haemorrhage in two, both premature.

Petechial haemorrhages of the pericardium and/or pleura occurred in 16 of the premature cases and 13 of the non-premature cases, 47% and 56.5% respectively, compared with 28.5% and 43.5% in the assigned causes group.

The pulmonary findings are considered in more detail and summarised in Table I.

	No precise cause of death		Precise cause of death	
	Premature	Non-premature	Premature	Non-premature
	(34)	(23)	(14)	(32)
Respiratory tree				
Mucoid fluid	2	7	4	4
Milk	-	2	-	-
Pus	-	-	2	2
Lungs				
Atelectasis	22(65%)	15(65%)	5(35%)	9(28%)
Broncho-pneumonia	-	1	1	4
Pleurae				
Petechiae	6	8	1	6
Pleural cavities				
Effusion	3	2	-	-
Empyema	-	-	-	4

Table I. Macroscopic findings in the respiratory system

Congestion was almost universal. In 65% of cases where no precise cause of death was found, there was atelectasis; in the group with a precise cause of death, this was not such a frequent finding (30%). There was a higher incidence of atelectasis in those born by caesarian section compared with those born by via naturales as shown (in percentages) in Table II.

Mode of delivery	No precise cause of death		Precise cause of death	
	Premature	Non-premature	Premature	Non-premature
Via naturales	61	44	28	-
Caesarian section	75	100	7	-

Table II. Incidence (percentage) of atelectasis in those born by via naturales and by caesarian section

There was no evidence in this series of inhalation of milk in any quantity; only an occasional case showed pleural effusion, in 4 cases of pneumonia in non-premature infants there was a complicating empyema.

Other organs showed congestion in most cases, but in the indefinite cause of death group there was little else of note, in occasional cases there were minor developmental defects, in 4 cases an ascites was present and in 3 adrenal haemorrhage was noted. In those dying of a precise cause, the pathological changes of these causes were evident.

B. HISTOLOGICAL FINDINGS

Histological material was not always taken, particularly in cases where a precise cause of death was demonstrated macroscopically at autopsy; 26 premature cases and 31 non-premature cases had this additional information.

a. The Lungs. The salient features regarding the pulmonary findings are summarised in Table III.

Finding	No precise cause of death		Precise cause of death	
	Premature	Non-premature	Premature	Non-premature
	(17)	(16)	(9)	(15)
Gross Congestion	11(65)	11(69)	6(67)	9(60)

Finding	No precise cause of death		Precise cause of death	
	Premature	Non-premature	Premature	Non-premature
Atelectasis	14(83)	13(81)	6(67)	6(40)
Widespread	8(47	10(63)	4(44)	2(13)
Partial	6(35)	3(19)	2(22)	4(27)
Emphysema	11(65)	7(44)	4(44)	4(27)
Widespread	6(35)	4(25)	3(33)	3(20)
Partial	5(30)	3(19)	1(11)	1(7)
Haemorrhage	2(12)	2(13)	3(33)	3(20)
Desquamated epithelium	1(6)	4(25)	2(22)	1(7)
Inflammatory infiltration				
Polymorphs	3(17)	-	4(44)	2(13)
Mononuclears	5(30)	3(19)	1(11)	4(27)
Exudate	11(65)	8(50)	4(44)	4(27)
Squames	4(24)	7(44)	2(22)	1(7)
Hyaline Membrane	9(53)	6(38)	3(33)	1(7)

Table III. Salient features in the pulmonary histology in 57 cases of neonatal death (percentages in parenthesis)

ATELECTASIS

Atelectasis was a prominent feature in some two-thirds of the material examined, being particularly evident (82%) in cases with no precise cause of death. The incidence was 50% in those with a definite cause of death, two-thirds of these being in premature infants. It was invariably present on microscopic examination in infants dying after delivery by caesarian section, irrespective of the indications for this operation.

EMPHYSEMA

Emphysema was noted to some degree in 45% of the cases, the maximum incidence being in premature infants with no precise cause of death (65%), the least in non-premature infants in whom a frank cause of death was found (27%). It was generally associated with partial atelectasis.

DESQUAMATION OF BRONCHIAL EPITHELIUM

Epithelial desquamation of the bronchi and bronchioles was not a frequent finding (14% overall) and was of 2 types. In some cases, bronchi showed an intact epithelium, but the lumen contained masses of epithelium derived from other areas. The other type showed disruption of the epithelium which lay in clumps in the lumen, the walls being devoid of lining cells. Both types were associated with some atelectasis.

INFECTIVE FEATURES

Infective features, as shown by the infiltration of polymorphonuclear cells, were seen to a greater or less degree in 22 cases (over one-third), the incidence being much the same whether the cause of death was precise or not. Frank pneumonic consolidation was seen in 5 cases, in 4 of which widespread and severe pneumonia without pathological changes elsewhere led to the conclusion that this was the primary cause of death. The fifth case showed scattered consolidated areas associated with death in a pre-viable infant and this, no doubt, hastened the end.

HYALINE MEMBRANE FORMATION

Hyaline membrane formation, incipient or frank, was seen in one-third of the cases examined histologically, being more frequent (46%) in the premature group than in full-term infants (22%). It did not, however, appear to be significant with any particular cause of death, being associated with cases in which there was no precise cause of death, with traumatic delivery and with maternal ante-partum haemorrhage, both in cases delivered naturally or by caesarian section. In most cases some degree of atelectasis was also present, frequently with other changes such as bronchial desquamation, emphysema, infective features and inhalation of liquor amnii.

b. The Liver. Material for histological examination of the liver was available in 23 cases, from 10 premature and 13 non-premature

infants. Congestion was almost universal; foci of haemopoesis were usually seen and degenerative changes were present in almost half the cases. Signs of more specific pathological change, however, were only seen in one case. This was a full-term infant (Case 7) who appeared normal for 3 days and then developed respiratory symptoms and died on the twelfth day of life. The lungs showed vascular changes, interpreted as an example of Ayerza's disease, the liver showed areas of fibrosis.

The extent of haemopoetic foci varied, it was assessed as being from none to intense and the degree in relation to birth weight is shown in Table IV.

Birth Weight	Degree of haemopoesis					Total with haemo-poesis	No of cases examined
	None	Slight	Moderate	Marked	Intense		
Less than 2lbs 8ozs	-	-	-	2	-	2	2
2lbs 9ozs- 3lbs 8ozs	2	-	1	2	-	3	5
3lbs 9ozs-4lbs 8ozs	-	1	-	1	-	2	2
4lbs 9ozs-5lbs 8ozs	-	-	-	-	1	1	1
Total,premature	2	1	1	5	1	8	10
Over 5lbs 8ozs	3	3	4	3	-	10	13
Total, neonates	5	4	5	8	1	18 (78.2%)	23

Table IV. Extent of Haemopoesis in liver sections of 23 neonatal infants in relation to birth weight

While haemopoetic activity was generally present (78.2%) there does not appear to be any correlation between the extent of this activity and the maturity of the infant as judged by the birth weight.

It may be noted that remnants of haemopoesis were seen in some of the older infants, occurring in 6 out of 27 liver sections examined; all were

seen in cases of sudden death in apparently normal infants.

c. The Pancreas. The pancreas showed foci of haemopoesis in 2 cases of erythroblastosis neonatorum in premature babies examined; there was some pancreatic fibrosis in a case of an infant dying from birth trauma, but there was no other evidence of mucoviscidosis; the pancreas in other cases showed nothing of note.

d. The Pituitary Gland. The pituitary gland was seldom examined histologically; haemopoesis was seen in a case of erythroblastosis.

e. The Testis. In only one case did a testes appear abnormal macroscopically, histological examination revealed an angioma. This was an incidental finding in an infant who died from birth trauma.

f. The Kidneys. The histological findings in the kidneys were mainly negative in character. In the premature group the kidneys from 2 cases of erythroblastosis neonatorum showed areas of haemopoesis. Conspicuous blood casts were seen in the distal tubules of a non-premature infant who died from birth trauma and in the case of Ayerza's disease the glomeruli of the kidneys showed swelling, often occluding the glomerular space.

g. The Adrenal glands. The adrenal glands in general showed little pathological change. In one case of a premature infant dying from birth trauma, sections of the adrenal showed thickening of the fibrous tissue capsule and almost complete absence of cortical tissue. In the cases of erythroblastosis, the cells showed much lipid material and haemopoetic activity was noted. Widespread adrenal haemorrhage was seen in 3 cases dying from birth trauma.

h. The Brain. Histological examination of the central nervous system (confined to the examination of sections stained by haematoxylin and eosin) did not add much to the autopsy findings. Haemorrhage was noted in one case of erythroblastosis and in the case of Ayerza's disease haemorrhage of some standing, as evidenced by the numerous reactive

gitter cells, was noted. Clumps of staphylococci were seen in sections of the brain from a case of staphylococcal septicaemia.

i. The Thyroid Gland. An attempt was made to assess the amount of colloid in the thryoid gland in relation to birth weight, age at death and cause of death, but no correlation appeared to be present.

Maturity	Cause of death	Age at death (in days)	Thyroid acini	Case
Premature	Not precise	1	Empty	123
Premature	Erythroblastosis	1	Distended with colloid	194
Full-term	Pneumonia	6	Colloid present	227
Full-term	Birth trauma	4	Empty	20
Full-term	Not precise(after caesarian section)	1	Active colloid absorption	73
Full-term	Not precise(after caesarian section)	1	Empty	192
Full-term	Ayerza's disease	10	Active colloid absorption	7
Full-term	Not precise	2	Empty	40

j. The Myocardium. Histological lesions of the myocardium were rare. In the case of staphylococcal septicaemia the heart muscle showed micro-abscesses. Focal myocarditis was an unexpected finding in a very premature infant who survived less than 24 hours, the lungs showed atelectasis, but no inflammatory infiltration, the myocardium showed conspicuous collections of polymorph leucocytes. Degenerative changes, generally of a minor character, were seen in a number of cases, fairly severe vacuolisation of the myofibrils and nuclear swelling was seen in an infant who died from erythroblastosis. In the asphyxial type of death, myocardial congestion was often marked.

k. The Thymus Gland. The thymus glad was examined histologically in only 6 cases, all showed congestion and 4 showed infiltration of the trabeculae

by eosinophilic leucocytes, the significance of which, in the few cases, was undetermined.

l. The Spleen. The spleen, examined histologically in 19 cases, frequently showed congestion, but little else of note (haemopoetic foci were seen in the cases of erythroblastosis).

m. Other Organs. In a few instances the intestinal tract, ovaries, uterus, placenta and lymph nodes were examined histologically but, apart from congestion in some cases, no pathological change was evident.

PART 2 - THE CLINICAL PICTURE

Some complicating maternal, foetal or obstetric factor was recognised clinically in 28 (58.6%) of the premature infants and in 36 (63.1%) of the non-premature group. These factors are summarised in Table V.

Factors	Premature Infants	Non-premature infants	Totals
Maternal			
Antepartum haemorrhage	8	2	10
Toxaemia of pregnancy	5	6	11
Pelvic disproportion	1	1	2
Previous caesarian section	-	1	1
Uterine fibroids	1	-	1
Elderly primipara	-	1	1
Tuberculosis	1	-	1
Pyelitis	2	-	2
Diabetes	-	2	2
Rhesus sensitisation	2	2	4
Hydramnios	-	2	2
Totals	20	17	37

Factors	Premature Infants	Non-premature infants	Totals
Foetal			
Multiple pregnancy	3	-	1
Congenital defects	1	10	11
Erythroblastosis	2	2	4
Post-maturity	-	2	2
Anaemia neonatorum	-	1	1
Ascites	-	1	1
Distress	1	2	3
Totals	7	18	25
Delivery			
Precipitate labour	3	1	4
Arrest with forceps delivery	2	1	3
Breech presentation	3	2	5
Caesarian section	8	7	15
"Born in a caul"	-	1	1
Cord round neck	-	1	1
Totals	16	13	29

Table V. Maternal, foetal and delivery factors recognised clinically in 103 cases of neonatal death

(Note: The totals do not represent cases as multiple factors were present in some instances)

The presence or absence of maternal, foetal and delivery factors has been correlated with the cause of death in Table VI.

Cause of death		No factors known	Factors present
Birth trauma	Premature	3	3
	Full-term	2	5
Frank infections	Premature	1	2
	Full-term	4	3

Cause of death		No factors known	Factors present
Congenital Disease	Premature	2	1
	Full-term	5	10
Erythroblastosis	Premature	-	2
	Full-term	-	2
Trauma	Full-term	1	-
No precise cause	Premature	14	20
	Full-term	8	15
Totals	Premature	20	28
	Full-term	19	36

Table VI. Presence or absence of maternal, foetal or delivery factors in relation to the cause of death

While maternal and delivery factors were evident more or less equally in the premature and non-premature group (Table V), there is a preponderance of foetal factors in the non-premature group compared with the premature one, due to congenital defects.

The principal symptoms and signs shown by these babies were generally respiratory in nature, with often difficulty in establishing proper breathing, followed by cyanotic attacks and in many cases apnoeic episodes leading to death. In the birth trauma group, only 6 out of the 13 cases showed cerebral symptoms, the remainder showed respiratory embarrassment and failure. In the majority of infective cases there was a period, from 2 to 7 days, when the baby's progress was satisfactory, the illness was then manifest by lethargy, cyanosis, rapid deterioration and in some cases abnormal signs in the chest. A picture of respiratory embarrassment was seen in nearly all the cases dying from congenital defects; in 11 cases out of the 18 there was clinical evidence of some such abnormality, generally cardiac, in addition. Very much the same pulmonary syndrome was seen in those in which no precise cause of death was found, the clinical picture did not show any appreciable difference

between infants who were premature or full term, nor between those with a history of some adverse factor and those without such a history. The cases of erythroblastosis were an exception in that they exhibited the classical syndrome of this condition. In general, therefore, the clinical picture presented by these infants was not specific nor diagnostic of any particular condition.

Analysis of the sex distribution is shown in Table VII, overall the sex ratio males/females was 1.3/4/1.

Cause of death	Premature		Non-premature		Totals	
	Male	Female	Male	Female	Male	Female
Birth trauma	3	3	6	1	9	4
Infective processes	2	1	1	5	4	6
Congenital deformity	1	2	9	6	10	8
Erythroblastosis	1	1	1	1	2	2
Trauma (other than birth injury)	-	-	-	1	-	1
No precise cause						
Adverse factors present	12	8	8	7	20	15
No known adverse factors	11	3	3	5	14	8
Totals	30	18	29	26	59	44

Table VII. Sex distribution in 103 neonatal deaths

The ages at death are shown in Table VIII

Day	Premature	Non-premature	Totals
1	23	23	46
2	9	9	18
3	8	4	12
4	3	2	5
5	1	5	6
6	1	2	3
7	-	-	-

Day	Premature	Non-premature	Totals
8	1	1	2
9	-	2	2
10	2	5	7
11	-	2	2
Totals	48	55	103

Table VIII. Ages at death in 103 cases

45% of the infants died within 24 hours of birth, 62%, 74%, 79% and 85% had succumbed by the second, third, fourth and fifth day respectively. There did not appear to be any great difference in survival time between the premature and non-premature groups, 92% of the former and 79% of the latter being dead by the fifth day. The 5 infants in the non-premature group who survived until the tenth day showed different causes of death (2 in the negative clinico-pathological group, one in the negative pathological group, one with congenital defect and one suffering from erythroblastosis foetalis).

Of the infants who died within 24 hours of birth 66% of the premature group and 58% of the non-premature group died within 6 hours of delivery and 98% and 95% respectively within the first 12 hours of life.

PART 3 - THE CLINICO-PATHOLOGICAL PICTURE

Consideration of the preceding two Parts enables one to conclude that no specific interpretation can be made in many neonatal deaths on the general gross or microscopic findings at autopsy. In the absence of clinical detail one could arrive, for instance, at a diagnosis of erythroblastosis foetalis by the finding of widespread haemopoetic foci in various organs, but one could not reach this conclusion from study of the liver alone, as extensive haemopoesis may be found there in deaths from other causes.

The finding of cerebral haemorrhage associated with a tentorial tear enables a diagnosis of birth trauma to be made, but cerebral haemorrhage without evidence of internal trauma may be found in what appear to be asphyxial deaths. Evidence of pulmonary infection may be so widespread as to enable one to conclude that pneumonia was the cause of death, but general pulmonary pathological changes such as minor infective features and hyaline membrane formation can be found in a wide variety of conditions.

These examples, and the wider illustrations preceding them, bear out the contention made in the Preamble that much the same morbid anatomical and histological picture may be found in a wide range of causes of death involving maternal, obstetrical or foetal factors or without any obvious clinical factors.

So that in attempting to arrive at a meaningful classification, the whole clinico-pathological picture must be considered. Even then there remains a group of cases (21.3% in this series) in which no obstetrical, labour or foetal factors could be incriminated and at autopsy only general pathological changes, particularly congestion and pulmonary atelectasis, could be found.

The main clinico-pathological groups in this series are as follows:

A. BIRTH TRAUMA

A diagnosis of birth trauma was made when widespread intracranial haemorrhage was found, generally associated with obvious trauma to intracranial structures, particularly tears in the tentorium cerebelli or the falx cerebri. On occasion no such tear was demonstrated, but the extent of subarachnoid haemorrhage in these cases was such as to lead to the conclusion that meningeal veins had been damaged. A few instances where haemorrhage was confined to the lateral cerebral ventricles were not included in this cause of death, intraventricular haemorrhage alone being

interpreted as an asphyxial phenomenon.

Of the 13 cases in this birth trauma group, significant maternal, delivery or foetal factors were recorded in 8 instances, minor foetal abnormalities, which may reflect some interference with viability, were present in 4 and no deleterious factors were known in one case. The incidence of significant factors was higher in the non-premature infants (5 out of 7 cases) than in the premature group (3 out of 6).

The main signs pertained to the pulmonary system, in only about half the cases were signs present which led to a provisional clinical diagnosis of cerebral complications. The sexes of the infants were almost equally represented, and as a rule the infants survived some time, only 3 out of the 13 dying on the first day of life, compared with 45% dying on the first day in the whole series of 103 deaths.

Widespread intracranial haemorrhage was demonstrated in all these cases, with definite tentorial tears in 5. Histologically the lungs (examined in 9 cases) showed atelectasis in 6, with hyaline membrane formation in 2, one of which also showed infective features. Two showed frank broncho-pneumonia. In only one case did the lungs appear histologically normal.

The incidence of birth trauma as a cause of death in this series (10.7%) is comparable to that reported at the University College Hospital, London, during the years 1948-55 (Bound et al, 1956).

B. FRANK INFECTIVE PROCESSES

Eight of the 10 cases included under the heading of frank infective processes were of neonatal pneumonia diagnosed as such when macroscopic and microscopic findings were deemed unequivocal of acute pulmonary infection in the absence of other abnormalities sufficient to prove fatal. (This definition is necessary as pneumonia is frequently found as a

complicating factor in other severe conditions, for example gross congenital malformations; such defects are considered the primary cause of death.)

Two cases occurred in premature infants, in both of whom possible deleterious maternal factors were present (one mother had a poor medical history, including mitral valvular disease and had suffered from bronchopneumonia and tuberculous cervical adenitis during the pregnancy, the other was an elderly patient who had had a normal delivery 14 years previously, then 3 miscarriages and the present pregnancy included a period of threatened abortion). In these 2 cases there were no untoward delivery factors and both infants appeared normal at birth. Clinically one showed a slow response from the beginning, culminating in cyanotic attacks and hyperpyrexia, the other was well and appeared to be thriving for 2 days, then became grey and lethargic. In both cases the lungs showed bronchopneumonia changes, confluent in areas, with pus in the bronchi. Apart from an undescended testicle in one infant, the remainder of the autopsies showed nothing of note.

Of the 6 cases of neonatal pneumonia occurring in non-premature infants, the maternal history was uneventful in all but one, in which a mother developed an influenzal-like illness shortly after parturition. One infant was born as a breech presentation, another as a face presentation, but all were delivered spontaneously. Survival time varied from 2 to 8 days. In 4 cases the infants appeared to thrive for several days, then clinical symptoms appeared. In one case (whose mother had influenza) there were early signs of an upper respiratory tract infection which progressed into signs of penumonia. The final case did not thrive, vomited after each feed and was lethargic with shallow respirations from the outset. This infant's head was of an odd shape, suggesting some degree of anencephaly, the remaining infants appeared physically normal. The clinical picture varied in the 4 who developed symptoms some time after birth; one had diarrhoea

and deteriorated rapidly, one developed listlessness and hyperpyrexia, one became cyanosed and the fourth developed signs of a severe respiratory tract infection which failed to respond to treatment. In all cases the lungs showed patchy or confluent consolidation with pus in the bronchi, one autopsy showed the presence of pulmonary abscesses. There was pleural involvement in 3, one with empyemata, and in all acute pneumonic changes were seen microscopically. In one child an incidental finding was a small intraventricular septal defect.

A case of staphylococcal septicaemia occurred in a premature infant who showed a congenital defect of the left hand. The infant's condition seemed satisfactory for 7 days after an uncomplicated delivery, but it then became cyanosed, developed respiratory distress, and died. Autopsy revealed petechial haemorrhages throughout the pencardium and lungs, with early inflammatory changes in the various sinuses in the skull. Microscopically, abscesses containing organisms morphologically resembling a staphylococcus were seen in the venous sinus thrombi, the myocardium and the lungs.

The case finally considered to be a viral hepatitis caused some diagnostic difficulty. This non-premature infant was born spontaneously from a mother who was Rhesus-negative and whose serum contained weak Rh-antibody. Shortly after birth the child became deeply jaundiced with a haemoglobin value of 94% and a serum bilirubin figure, terminally of 35 mgm per 100 ml. The direct Coomb's test, however, was negative. The liver and spleen were enlarged, but there was no kernicterus. Microscopically there was no evidence of erythroblastosis, the liver showed intralobular necrosis with a polymorph leucocyte infiltration. The lungs showed early pneumonic changes.

C. CONGENITAL DISEASE

1. The direct cause of death

In 18 cases (17.5%), death was attributed primarily to congenital defect, this incidence being comparable to the figure of 18.1% quoted by Bound et al (1956). This cause of death showed a higher incidence in non-premature infants (some 14.5%) than in premature babies (some 3%) and indeed was one of the major factors producing death in the former (accounting for nearly one-quarter of the deaths in that group).

The systems affected were:

	Premature infants	Non-premature
Cardio-vascular	2	9
Intestinal	1	1
Hepatic		1
Renal (agenesis)		1
Gross deformity		1
Pulmonary (agenesis with diaphragmatic hernia)		1
Exomphalos		1
	3	15

The main defects occurred in the cardio-vascular system, single examples of a wide range of other deformities being found. It is noteworthy, in contrast to the findings of Bound et al (1956), in which nearly one-third of congenital defects causing death in stillborn infants or neonates were of the central nervous system, that cases of such a nature (5) in the present series caused death in the post-neonatal period and are recorded in Chapter II.

Maternal and delivery factors were virtually absent in these cases. In one case of cardiac abnormality, the infant was one of undiagnosed twins, the second being born macerated. One infant was delivered by low forceps, the remaining deliveries were spontaneous.

In most cases of cardio-vascular abnormality, the clinical picture was that of cyanotic attacks and in about half the cases there were abnormalities detected during life in heart size or in electrocardiographic tracings. In the case of diaphragmatic hernia, normal respirations were not established and the infant died about one hour after delivery. The intestinal cases (one of gross pyloric stenosis and one of atresia of the ileum) showed continuous vomiting and survived 2 and 5 days respectively. The renal agenesis case was born in a state of asphyxia livida and survived only a few hours, the exomphalos and gross deformity cases were self-evident and survived a few hours. The case of atresia of the common bile duct (which also showed right ventricular hypertrophy with no anatomical cardiac defect) showed progressive jaundice and died on the tenth day of life.

The cardiac abnormalities included transposition of the great vessels (2 cases), high intraventricular septal defect with common arterial trunk (1), congenital coarctation of the aorta (3) with or without septal defect, anomalous pulmonary arteries (2), anomalous tricuspid valve (1) and absence of the intra-atrial septum(1). A final case, in which the left ventricle showed considerable hypertrophy, but no anatomical defect was demonstrated in the heart, showed gross proliferative endarterites of the small vessels of the lung microscopically and has been diagnosed as a case of Ayerza's disease. Apart from this case, histological examination showed little abnormality in the rare cases in which it was performed in this group.

2. Incidental findings

Apart from gross conginital malformations judged to be the primary cause of death, minor defects were noted in a further 18 cases, the total incidence of congenital defects being shown in Table IX.

	As direct cause of death				As incidental findings				Overall total	
	Cardiac	Other	Total	%	Cardiac	Other	Total	%	Number	%
Premature	2	1	3	6.2	2	5	7	14.6	10	21
Non-premature	9	6	15	27.3	6	5	11	20	26	47.3
Totals	11	7	18	17.5	8	10	18	17	36	29

Table IX. Incidence of congenital disease in 103 neonatal deaths

The incidental findings were:

Premature infants		Non-premature infants	
Hypospadias	1	Hypospadias	1
Intra-atrial septal defect	2	Patent foramen ovale	5
Talipes	1	Intraventricular septal defect	1
Cyst of liver	1	Talipes	1
Malrotation of gut	1	Multiple defects	1
Absent bones of forearm	1	Pilonidal sinus	1
Anomalous ribs	1		

It is noteworthy that the overall incidence of congenital defects, major and minor, in this series of 103 neonatal deaths amounted to 29%, nearly one-third.

D. ERYTHROBLASTOSIS NEONATORUM

Erythroblastosis caused the death of 2 premature infants and of 2 in the non-premature group. All were fairly typical examples of this condition with anaemia, high blood bilirubin levels and jaundice, enlarged liver and spleen, oedema and positive direct Coomb's tests.

At autopsy these clinical findings were confirmed, effusions into serous cavities and numerous petechial haemorrhages into various organs were noted. Microscopically (2 cases examined) widespread erythroblastic activity was seen in many organs including the liver, lungs, spleen,

kidneys, adrenals and pituitary. One case showed marked lipid deposition in the cortical cells of the adrenal and in one case the lungs showed incipient hyaline membrane formation.

Maternal histories showed that the mothers were rhesus-negative with Rh antibodies in their serum and 2 cases in addition suffered from mild pre-eclamptic toxaemia. Two infants were delivered spontaneously, 2 by caesarian section; survival times varied from $\frac{1}{2}$ - 8 hours.

E. TRAUMA OTHER THAN BIRTH INJURY

A normal baby returning home with her mother after discharge from hospital on the tenth day of life was killed in a road traffic accident, the cause of death being multiple injuries.

F. NO PRECISE PATHOLOGICAL CAUSE OF DEATH

1. Maternal, labour or foetal factors present

A group of 35 infants (20 premature, 15 non-premature) who all had some important maternal, delivery or foetal complication present, did not show any precise cause of death. Autopsy (including histological examination in a considerable number) showed a non-specific picture which included widespread congestion, sometimes petechial haemorrhages in various organs, often complete or partial pulmonary atelectasis frequently associated with evidence of inhalation of liquor amnii and incipient or frank hyaline membrane formation.

The clinical picture could be divided into 2 main patterns. In one group (10 premature and 5 non-premature infants), the babies were delivered in varying states of asphyxia which did not respond to treatment; in the second group (9 premature and 10 non-premature) respiration was satisfactorily established naturally or after treatment of initial asphyxia, but after a few hours (days in one case) respiratory distress became evident and death occurred within a few hours or days. An exception was a premature infant

who appeared to be progressing after resuscitation, but was found dead in its cot 30 hours later. This infant's twin had a history of the second main group mentioned.

More than half of these infants did not survive one day. Twelve of the premature and 8 of the non-premature babies were born per via naturales, with or without instrumental assistance, the remainder were delivered by caesarian section. The associated maternal, delivery and foetal factors are shown in Table V for the whole series of 103 infants.

2. Maternal, labour or foetal factors absent

There remained a group of 22 cases (14 premature, 8 non-premature) in which the pathological findings and the neonatal clinical course closely paralleled that in the previous group, but in which there were no recognised adverse maternal, delivery or foetal factors. The greater proportion of these were premature, but apart from one extremely premature infant (birth weight 1 lb 6½ ozs) the birth-weights were within limits of expected compatibility with life. Six infants (4 premature) showed immediate post-delivery asphyxia which did not respond, 10 (all premature) showed the delayed type of respiratory distress, 5 died suddenly on the 5th - 12th day and one failed to thrive and died in a marasmic state on the 12th day of life.

Autopsy in all these cases showed the same non-specific asphyxial picture.

3. Conclusions on groups F1 and 2 above

Early neonatal asphyxia is a well-recognised condition. In the case of infants who initially appear satisfactory or respond to resuscitation and then relapse, again the syndrome is well recognised as the respiratory distress syndrome although the mechanism is not yet clear (see discussion in Chapter 5). The sudden deaths in 6 infants did not show the infective features found in so many deaths of this type in the older infant and may be

fulminant cases of the respiratory distress syndrome. No reason was discovered for the marasmic state of one infant.

PART 4 - CLASSIFICATION OF NEONATAL DEATH

Consideration of the clinico-pathological picture in this series of 103 neonatal deaths leads to the following simple classification:

Causes of neonatal death	Figures in this series
1. Birth trauma	13
2. Infection	10
3. Congenital malformation	18
4. Erythroblastosis foetalis	4
5. Neonatal asphyxia	21
6. Respiratory Distress syndrome	35
7. Miscellaneous	2(RTA 1 Marasmus 1)

Maternal, delivery or foetal factors should be specified where known.

CHAPTER 2

DEATH AFTER SERIOUS ILLNESS

"O fairest flower; no sooner blown than blasted,
Soft, silken primrose fading timelessly".

From an Ode on the Death of a Fair Infant Dying of a Cough

John Milton (1608-1674)

PREAMBLE

In 64 (25.6%) of the deaths in this series occurring after the 14th day of life there was a history of illness of over 6 hours duration and these form the material analysed in this Chapter.

PART 1 ANATOMICAL CAUSES OF DEATH

The primary causes of death, as decided by autopsy, are shown in Table X.

Cause of Death		Number	Percentage
Infection	Gastro-enteritis	18	28.1
	Respiratory	18	28.1
	Septicaemia	3	4.7
	Central Nervous System	5	7.8
	Meningitis	3	
	Encephalitis	1	
	Sinus Thrombosis	1	
	Hepatitis	1	
	Peritonitis	1	
	TOTAL, infection	46	71.9
Congenital	Cardio-Vascular	9	
	Central Nervous System	5	
	Intestinal	1	
	Hepatic	1	
	TOTAL, congenital	16	25

Cause of Death		Number	Percentage
Accidental	Aspirin poisoning	1	
	Trauma: Road Traffic Accident	1	
	TOTAL, accidental	2	3.1
	TOTAL, all causes	64	

Table X Causes of Death After Serious Illness In 64 Cases

It will be noted that about three-quarters of these infants died from infective processes, mainly gastro-enteritis and pneumonia. Congenital defects accounted for nearly all the remainder.

PART 2 EPIDEMIOLOGICAL DATA

There was a preponderance of males dying in this series, 41 to 23 females, a rate of nearly 1.8 to 1. Analysis of the sex and major causes of death is shown in Table XI.

	Infection				Congenital			Accidental
	Gastro Enteritis	Pneumonia	Other	All	Cardiac	Other	All	
Male	10	11	8	29	7	4	11	1
Female	8	7	2	17	2	3	5	1

Table XI Sex Of Infants Dying After Serious Illness

The male preponderance affects both the major groups of death, infection and congenital defect.

The age at death, under the major anatomical causes, is shown in Table XII.

Age in months	Infection			Congenital	Accidental	Total
	Intestinal	Respiratory	Other			
1	3	2	1	2		8
2	4	4	1	3		12
3	1	3	2	4		10
4	2	1		1		4
5	2	1	1	1		5
6	1		1			2
7	1	2	1			4
8	1			1		2
9	2			1		3
10		1	1			2
11	1	1				2
12			1			1
13-18		2	1	3	1	7
18-24		1			1	2

Table XII Age at Death in 64 Cases Of Serious Illness In Infancy

Nearly one-half of the deaths occurred in the first 3 months of life, the remainder showed no particularly vulnerable age.

The duration of illness, similarly tabulated under the major causes of death, is shown in Table XIII.

Duration of illness		Infection			Congenital	Accidental	Total
		Intestinal	Respiratory	Other			
Days	1	3	4	4	1	2	14
	2	1	5				6
	3	2	2	1	1(a)		6
	4	1	2	1	2(a)		6
	5	2			1		3
	6	1	1	1			3
	7	2	2	1			5
Weeks	1-2	3	1		2(a)		6
	2-3	1			1		2
	3-4	1		1			2
Months	1-2		1	1	4		6
	2-3				3		3
over 3					1		1
Not stated		1					1

Table XIII Duration Of Illness in 64 Infants Dying After Serious Illness

(Note (a) Some of these infants were in poor health all their lives, the period of acute illness is recorded here).

The duration of illness in the great majority of cases dying from infective conditions was relatively short, 78% dying within one week of onset, whereas those dying from congenital defect showed a more protracted course, 60% surviving more than one week and 50% being ill for a month or longer.

The seasonal incidence of these deaths (excluding the 2 accidental causes) is shown in Table XIV.

Month of death	Infection			Congenital	Total
	Intestinal	Respiratory	Other		
January	1	1		1	3
February	1	2	2		5
March	1	6	1	1	9
April	1	3		2	6
May		1			1
June		1		4	5
July	3	1	2	2	8
August	1	2		1	4
September	2		1	3	6
October	2		2	2	6
November	3				3
December	3	1	2		6

Table XIV Seasonal Incidence of Death In 62 Seriously Ill Infants

Comparing the colder (October-March) and warmer (April-September) periods, there is little difference in the incidence of infective conditions; 12 of the 16 congenital cases died during the summer months.

PART 3 THE CLINICO - PATHOLOGICAL PICTURE

Brief clinical details and notes on the pathological findings at autopsy in the infective and congenital groups are tabulated in Appendix B. An analysis of these cases, with illustrative case histories, follows.

A. GASTRO-ENTERITIS

Gastro-enteritis accounted for 18 deaths (28.12%) in this group of 64 seriously-ill infants. In 10 cases the clinical history was only that of diarrhoea and vomiting, with, in general, the development of dehydration

which did not respond to parenteral fluid therapy and antibiotics, or in some cases initial response to these measures with subsequent relapse. Six of these cases were of relatively short duration, the period of symptoms lasting from one day's severe, almost choleriac-like diarrhoea with vomiting, to 5 days symptoms of increasing severity. The remaining 4 cases had protracted illnesses of 2-4 weeks duration with gradual deterioration and death in a marasmic state.

In the other 8 cases there were, in addition to diarrhoea and vomiting, symptoms or clinical signs relating to other than the gastro-intestinal tract, although death was attributed primarily to gastro-enteritis. Two had concomitant signs indicating pulmonary infection, 3 had a history of upper respiratory tract infection 4-13 days previously which had apparently resolved before the intestinal symptoms developed, one had parotitis and bilateral otitis media with terminal signs of a basal pulmonary infection and the remaining 2 developed diarrhoea and vomiting a few days after minor surgical procedures (circumcision). In one of these symptoms suggested obstruction, but laparotomy did not substantiate this, showing only a blood-stained ascites.

The age at death varied from 4 weeks to 11 months, but in this small series of cases there did not appear to be any correlation between age and type of gastro-enteritis (acute, chronic or complicated); the majority (13 out of 18) occurred in the age group of 6 months or less (table XII). There did not appear to be any definite seasonal trend, 10 of the cases occurring during the colder period, October-March and 8 between April-September (Table XIII).

No pathogenic organisms are recorded as having been isolated from specimens of faeces during life, nor from intestinal swabs taken at autopsy.

The morbid anatomical and histological findings can be illustrated by

the following cases:

Acute gastro-enteritis. A 9 month old infant (case 158) had been vomiting for over 2 days, then developed diarrhoea and when first seen by a doctor was seriously ill, semi-comatose with signs of severe dehydration. Some improvement followed therapy with antibiotics, oxygen and parenteral fluids, but the child collapsed and died 5½ hours after admission to hospital.

At autopsy, signs of dehydration were marked. The lungs showed basal congestion, the intestines were congested and dilated, the mesenteric lymph nodes enlarged and the liver yellow in colour. Histologically, the lungs showed patchy emphysema and oedema. The small intestine showed an exudate containing polymorphs and macrophages in the lumen and the wall showed conspicuous lymphoid tissue with a surrounding infiltration of acute inflammatory cells. The parenchymal cells of the liver showed fine vacualisation. The kidneys, which appeared normal naked-eye, revealed swollen glomeruli and swelling of the tubular epithelium and an area of fibroblastic tissue in the boundary zone between cortex and medulla, with proliferation of the epithelium of nearby tubules. These renal changes indicate the development of a lower nephron nephrosis consequent upon the fluid and electrolytic upset.

Chronic gastro-enteritis. An infant (Case 224) developed diarrhoea and vomiting 3 weeks after birth and was admitted to hospital one week later in a dehydrated, marasmic state. The haemoglobin level was 53%, despite dehydration, and the urine contained albumen. Improvement followed treatment, the albuminuria disappeared, but frequent relapses of diarrhoea followed; the chest remained clinically unaffected throughout and the infant succumbed after an illness lasting, in all, one month.

Post-mortem revealed an emaciated baby. There were haemorrhages into the mucosa of stomach and duodenum, the intestines were distended and extremely thin-walled, slight ascites was present. Histologically the gastro-intestinal tract revealed little of note beyond an area of deep necrosis in the stomach wall with commencing abscess formation. The lungs, however, contained areas of consolidation with micro-abscesses containing large and small mononuclear cells and polymorphs. Other organs showed degenerative changes.

These findings were interpreted as a terminal pneumonia following protracted gastro-intestinal infection.

Acute gastro-enteritis with concomitant respiratory signs. One case (102) occurred in a 7 month old baby who died in a state of gross dehydration 2 days after the onset of symptoms. Histological examination showed congested intestines, interstitial pneumonia, excess lipid in the adrenal glands and swollen glomeruli with degenerative tubular changes in the kidneys.

Another case of the same nature (104), where there was clinical evidence of broncho-pneumonia after a 3-day history of vomiting and diarrhoea in a 5-month old child, showed considerable vacuolisation of the liver cells, an acute interstitial pneumonia and, though the intestinal tract itself showed only congestion, the mesenteric lymph nodes were infiltrated with polymorph and macrophage cells.

Post-operative gastro-enteritis. Case 99 was of an infant, one month old, who developed gastro-enteritis after circumcision. The inflammatory infiltration of the intestine was largely eosinophilic, the liver showed vacuolated cells and remnants of haemopoesis.

In the other case of this nature (92), in which laparatory was carried

out because of the clinical suspicion of intestinal obstruction, histological examination of the lungs showed a minor peri-bronchial infiltration with polymorphs and macrophages, the small intestine showed an excess of polymorphs in the wall and the mesenteric lymph nodes were infiltrated with polymorphs and macrophages. The liver showed fatty change.

B. PNEUMONIA

Pneumonia caused the same number of deaths, 18 (28.12%) as did gastro-enteritis in this group. These cases will be divided into 4 main subgroups.

1. Pneumonia arising during the third to fourth week of life in babies which were born prematurely (the neonatal period dealt with in Chapter I has been taken as the first 14 days of life, hence these cases are considered here).

There were 3 cases in this category. The duration was short (2-4 days), one showed petechial haemorrhages, 2 had empyema associated with pulmonary abscesses, the third case was of mononuclear and giant cell type pneumonia. In all 3, a staphylococcus was identified. Other systems showed little of note, in one case there was haemorrhage into the adrenal glands (suggesting terminal septicaemia) and renal glomeruli showed swelling. These 3 cases arose in the warmer period April-September.

2. Pneumonia with no apparent contributory factors. Six cases fell into this subgroup, there was a wide variation in age at death (2-17 months), 2 were males, 4, females. The illness was of an acute nature (1-4 days) though minor symptoms were present in 2 cases 4 and 10 days before onset of the acute episode, with the exception of one case which ran a protracted course of intermittent illness for 7 weeks. Only one case showed petechial haemorrhages, one had empyema associated with a pulmonary abscess, 2 had serous pleural effusions. In the cases examined histologically, mononuclear

pneumonia was evident in 3 (one in addition to a pyogenic abscess) and plasma cell pneumonia in one. In only one case was a staphylococcus aureus isolated. Other systems showed little of note, one case had a concomitant otitis media, not evident during life, one showed renal changes with hyalinisation of some glomeruli and proliferation of Bowman's capsule, another showed a solitary cyst of the liver and one, evidence of liver inflammation suggesting the onset of septicaemia. Four of the 6 cases arose during the winter months.

One case (No 236) was in striking contrast to the acute episodes in the remainder and in view of the comparative rarity of this condition, pneumocystis pneumonia, in British medical practice it is described in some detail.

The patient, an 11-month old male infant, the son of a British sergeant, was in hospital from 21 January to 2 February 1960, with obstructive laryngo-tracheo-bronchitis which appeared to respond to treatment. A few days after discharge, he developed coughing with an expiratory grunt, his appetite was poor and the mother thought there had been a steady loss in weight. The coughing bouts often ended in vomiting, suggesting whooping cough, and the child was re-admitted to hospital on 21 March. He again appeared to improve on antibiotic therapy, but then relapsed with dyspnoea, intermittent paroxysmal cough and lethargy. His condition now rapidly worsened with the development of low-grade pyrexia, dyspnoea at rest and rapid pulse. The respirations were shallow, breath sounds loud, but there were no accompaniments; clinical examination of other systems showed nothing of note. The haemoglobin level was 69%, white blood cell count 11,000 per cu mm, 96% being lymphocytes. Culture of the sputum yielded a monilial organism and mixed bacterial flora of the commensal type. Despite a wide range of antibiotics and continuous oxygen therapy, the infant became very restless, relapsed into unconsciousness

with signs of peripheral cardiac failure and he died 3 days after the final admission to hospital, after an illness lasting intermittently for 7 weeks.

At autopsy the brain was noted to be oedematous. There was emphysema of the soft tissues of the auterior mediastinum, the right side of the heart was considerably dilated. The respiratory tree showed no obvious abnormality, the visceral pleura showed petechial haemorrhages. The lungs, pink in colour, felt hard, the right weighting 355g, the left 295g. The cut surface appeared solid with no evidence of aeration. Sections of the lungs showed, throughout, thickening of alveolar walls which were infiltrated by polymorphonuclear leucocytes, numerous plasma cells, often binucleate, macrophages and lymphocytes. The lumina of the alveoli were filled with a distinctive, foamy vacuolated material which had shrunk away from the walls, there were also a few mononuclear cells and scanty polymorphs. The bronchial walls sometimes showed epithelial desquamation and the same foamy material was seen in the lumen of some. This material gave a positive reaction with a periodic acid-Schiff stain and was interpreted as being the protozoon Pneumocystis carinii. Histological examination of other organs showed nothing of note.

3. Pulmonary complications of previous infective disease. In 5 cases there was a history of previous infection, but the complicating bronchopenumonia was judged the primary cause of death. Two cases were complications of measles, one followed a succession of illnesses including measles, one arose in an infant suffering from eczema and the final case had a previous history of mild enteritis which had not given rise to any anxiety. The ages of this subgroup ranged from 3 to 19 months and the length of illness from one day to one month, the acute phase lasting a week at the most.

At autopsy, one case showed cerebral petechiae, one had an empyema and 3 showed serous pleural effusions (sanguineous in one). The lungs in all

cases showed broncho-pneumonia (one with abscess formation), with areas also of mononuclear infiltration, 2 including giant cells and one showing hyaline membrane formation. In 2 cases a staphylococcus aureus was isolated. Three of these 5 cases occurred in the winter months.

4. The final 4 cases in this group of pneumonias presented some congenital abnormality, the pulmonary infection being gauged the cause of death. Two showed cardiac conditions, one was a mongol and the fourth case showed a hamartoma of the larynx. The infants' ages varied from 2 to 9 months at death, the final disease was of an acute nature lasting ½ - 2 days. Two showed petechiae of the pleura (one in addition of the pericardium) and 2 had serous pleural effusions. The type of pneumonia was lobar in 2, broncho-pneumonia in one and a mononuclear pneumonia in the fourth case. Three of these 4 cases occurred during the winter months.

5. Summary. Eighteen cases of pneumonia in infancy are analysed, 6(33%) did not appear to have any significant contributory factors, the remainder showed such factors (previous prematurity in 3, previous infection in 5 and congenital malformation in 4).

There did not appear to be any correlation between these subgroups and the age of the infant at death, apart from the post-prematurity cases.

Eleven cases occurred in males, 7 in females. The duration of the illness was generally short, at least the terminal pulmonary episode lasted only a few days. The case of pneumocystis pneumonia was an exception.

Signs of an acute asphyxial end (petechial haemorrhages) were seen in 5 instances, in only one case was there evidence, and that slight, of inhalation of stomach contents.

Pleurisy or empyema was present in 11 out of the 18 cases. The type of pneumonia varied. In cases examined histologically, 3 had abscess formation in broncho-pneumonia, 4 showed broncho-pneumonia (a polymorphonuclear response) and these 7 cases also showed areas of mononuclear pneumonia;

in a further 3 instances the pneumonia was of the mononuclear type, often with giant cells and in the final case examined histologically the pneumonia was predominantly of the plasma cell type associated with infection by Pneumocystis carinii. Pyogenic organisms (staphylococci) were isolated in 6 out of the 17 cases of acute pneumonia.

Two cases showed early nephritic changes, one an incidental cyst of the liver, cardiac abnormalities were present in 4, in 2 of which this condition was considered to be contributory to, but not the direct cause of, death.

Ten of the cases occurred in the colder months October-March: although at first sight there did not appear to be any material correlation between the season of incidence, it may be noted that if the post-prematurity group are excluded, 2 thirds of the cases of pneumonia arising de novo or as complications occurred during the winter months.

C. OTHER INFECTIVE CONDITIONS

Ten cases (15.62%) of the seriously-ill group of infants died from primary infective conditions other than gastro-enteritis or pneumonia. Illustrative cases follow.

1. Overwhelming septicaemic conditions. 3 cases. Case 163. A 16-day old female infant with jaundice, bradycardia and respiratory embarrassment. At autopsy salient findings were - suppurative choleangitis, myocarditis, nephritis, pleurisy, broncho-pneumonia and early abscess formation in the lungs. Clumps of organisms resembling a staphylococcus were seen in these areas and also, without any cellular reaction, in the adrenal gland. The umbilicus showed no evidence of infection.

Case 154. A 5-month old male child with diarrhoea and vomiting, but no evident dehydration, followed by lethargy and cyanosis. Main autopsy findings: Meningeal infiltration, oedema and congestion of the brain,

macrophage infiltration of paratracheal lymph nodes, interstitial pneumonia and fatty change in the liver. A Freidlander's bacillus was isolated from the heart blood and a bronchial swab and the findings were interpreted as an interstitial pneumonia and meningeal infection as part of a fulminating septicameia.

Case 13. A 7-week old male infant with respiratory embarrassment, multiple purpuric spots in the skin, and severe constitutional symptoms. White cell count was 14,000 per cu mm, 76% being polymorphs. Autopsy showed a diffuse petechial skin rash with petechial haemorrhages also in the mesentery. The lungs showed early mononuclear pneumonia, the cerebro-spinal fluid contained 12 white cells per cu mm but no other noteworthy findings. The suprarenal glands were haemorrhagic. Although no aetiological agent was isolated, the clinical history and meagre autopsy findings, but including suprarenal haemorrhages and slight increase in cells in the CSF, led one to conclude that this was probably an example of a meningococcal septicaemia giving rise to the Freidrich-Waterhouse syndrome.

2. Central nervous system infections. There were 5 examples of this comprising 3 cases of meningitis, one of encephalitis and one of a more obscure nature leading to longitudinal sinus thrombosis.

Case 119. An 18-month old infant who died after a short period of illness with signs of meningism. At autopsy there was a purulent meningitis and a section specially stained showed Gram-negative cocci although no organisms were isolated on culture. The lungs showed a mononuclear pneumonia, with incipient hyaline membrane formation, and the renal glomeruli were swollen. Although definite bacteriological proof was lacking, a diagnosis of meningococcal meningitis appeared justifiable on these findings.

Case 25 was of a similar nature in a 12 month old male infant; a strain of Neisseria meningitidis was isolated from the brain. The infant

had an acute illness with a haemorrhagic skin rash. At autopsy there was a purulent meningitis, small suprarenal haemorrhages, interstitial pneumonia infiltration of the liver with polymorphs and degeneration of the myocardium. This case has been put in the category of meningococcal meningitis as there was anatomical involvement of the meninges, features indicate a general septicaemic condition.

Case 208 concerned a 2-month old infant who died after a period of lethargy, lapsing into coma, with a bulging anterior fontanelle. Examination of the cerebro-spinal fluid during life confirmed the diagnosis of a meningococcal meningitis. At autopsy there was little to note beyond congestion of the meninges which were infiltrated with polymorph cells.

Case 111 was diagnosed as encephalitis though no virological confirmation was obtained. The infant had general symptoms with signs of dehydration, developed cyanosis then became semi-comatose and signs of peripheral circulatory failure ended in death, the clinical diagnosis being uncertain. At autopsy the brain showed congestion and there was a large intra-cerebellar haemorrhage. The cerebrum showed petechial harmorrhages and the lateral ventricles were full of blood clot. Histologically, the brain showed thrombosis of small vessels with haemorrhages and an infiltration of small round cells, polymorphs and macrophages. The meninges were unaffected and no neuronophagia was seen. A diagnosis of cerebeller haemorrhage due to encephalitis of unknown aetiology was made on these findings.

Case 87 was also of obscure origin. A 10-week old male infant developed pyrexia (to 105.4°F) after a period of restlessness and vomiting. The cerebro-spinal fluid was normal. The infant remained listless with no clinical localisation of a disease process and died suddenly. At autopsy there was considerable congestion of the brain with oedema of the meninges. No focal cerebral lesion was found, but the posterior part of the

longitudinal sinus showed ante-mortem clot. Histologically the brain showed thrombosis of vessels in this area, the wall of the longitudinal sinus showed haemorrhage and an infiltration of inflammatory cells. The lungs showed a mononuclear cell infiltration and the liver, fatty change.

There is some doubt as to the primary cause of death here, but it was judged an encephalitis of fulminant type, the only positive findings of note being longitudinal sinus thrombosis and thrombosis of small cerebral vessels.

3. One infant died from liver disease interpreted as being post-infective in nature. This infant, a 3 month old male, died in a German hospital after a 6 week's history of illness. The clinical details available are meagre and not illuminating. Autopsy, carried out at a British Military Hospital, showed an emaciated infant with oedema of the lower limbs, serous pericardial and pleural effusions and an ascites. The liver weighed 180 g and was coarsely granular with large masses protruding from the surface. Histological examination showed destruction of normal architecture, the essential feature being portal cirrhosis with nodular parenchymatous regeneration and marked small bile-duct proliferation. This was interpreted as a post-hepatitis cirrhosis rather than being of syphilitic or of non-infective origin.

4. The final case in the infective subgroup was that of a peritonitis with hepatic vein thrombosis. The infant (Case 45) was a 10-week old female. Previous history included a urinary infection 2 months previously and burns of the wrist 6 weeks before the development of pyrexia, vomiting, abdominal distension and marked hepatomegaly leading to death. During the terminal stages the white blood cell count rose to 26,000 per cu mm and the urine contained numerous pus cells and yielded a coliform organism on culture. At autopsy the main findings were bilateral pleural effusions, a purulent peritonitis and thrombosis of all the main branches of the hepatic vein.

The primary source of infection in this case may have been urinary in origin.

D. CONGENITAL DEFECTS

Sixteen cases (25% of those dying after serious illness) died from what was considered to be the direct effects of congenital malformation. An additional 9 cases, already mentioned under various headings, had congenital defects which were considered to be, at most, contributory to the death and not the primary cause. In all then, in this group of 64 infants dying after serious illness, 25 (almost 40%) had evidence of congenital defects which may be classified as follows:

	Number	Percentage
1. Congenital defect primarily responsible for death	16	25
Cardiac	9	
Central nervous system	5	
Intestinal	1	
Hepatic	1	
2. Congenital defects contributory to death	4	6.4
Cardiac) Death	2	
Mongolism) from	1	
Laryngeal hamartoma) pneumonia	1	
3. Congenital defects incidental to death	5	8.0
Cardiac (death from pneumonia)	3	
Cardiac (death from gastro-enteritis)	2	

TABLE XX: CLASSIFICATION OF CONGENITAL DEFECTS IN DEATH AFTER SERIOUS ILLNESS

Of these 25 congenital conditions 16 (64%) were cardiac in origin.

Congenital defects primarily responsible for death are illustrated by the following cases.

1. Cardiac abnormalities. Nine cases fell into this subgroup:

Case 151. A 3-month old infant developed dyspnoea, flaccid paralyses and loss of reflexes and died one day later. Autopsy showed coarctation of the aorta and bilateral talipes deformity. Histologically the congested lungs showed areas of acute emphysema and mononuclear cell infiltration. The kidneys showed fibrosis, cystic change, malformed glomeruli and inflammatory foci.

Case 240. An 18-day old female infant was found to have a loud pre-systolic murmur at neonatal examination. Cyanotic and apnoeic attacks became frequent before death. The heart consisted essentially of 2 chambers due to absence of the upper half of the intraventricular septum, the presence of a single auricle and a single arterial trunk, virtually a cor biloculare.

Case 187. A male infant, found to have a cardiac abnormality at neonatal examination, gradually deteriorated and died at the age of one month. Autopsy showed transposition of the great vessels with an intraventricular septal defect and abnormal distribution of the main arterial trunks.

Case 30. A male infant appeared well until 5 days before death when he developed "snuffles" and became pale and dyspoeic; respiratory movements weakened and he died at the age of 2 months. At autopsy the right ventricle was found to be obliterated by fibro-muscular hyperplasia with obliteration of the pulmonary and tricuspid values. A patent foramen ovale permitted a mixed circulation.

Case 247 was another example of transposition of the great vessels with a terminal episode of renal infarction. The infant had been cyanosed since birth, his brief life ran a stormy course throughout punctuated by episodes of pneumonia; he collapsed and died at the age of 2 months. In addition to the cardiac abnormality, the lungs showed mononuclear pneumonia and the right kidney was disorganised, with thrombosis of the renal vein.

Case 181. A male infant died at the age of 4 months after cyanotic and apnoeic attacks. He was mongoloid and at autopsy almost complete absence of the atrial and ventricular septae were found.

Case 141. A 7-month old male infant, cyanosed since birth, died after attacks of syncope. At autopsy the heart showed a Fallot's tetralogy defect.

Case 201. A male infant had been diagnosed as a case of transposition of the great vessels at Great Ormond Street Hospital. At the age of 17 months he developed diarrhoea and skin petechiae and died after a brief illness. The diagnosis of transposition of the great vessels, with intraventricular septal defect, was confirmed at autopsy although the clinical impression that the terminal episode was due to bacterial endocarditis was not substantiated. The lungs showed areas of emphysema, thrombosed vessels and pneumonic patches.

Case 234. A female infant died at the age of 19 months after a history of repeated respiratory infections. At autopsy there was widespread pneumonia with bilateral pleural effusions, but the cardiac defect was considered the primary cause of death. This consisted of an anomalous coronary artery distribution, the left coronary artery arising from the pulmonary artery and the grossly hypertrophied heart showed endocardial fibro-elastosis; there was also coarctation of the aorta. The lungs showed patches of purulent broncho-pneumonia.

2. Abnormalities of the Central Nervous system

In 5 cases abnormalities of the central nervous system were the cause

of death. In 4 the anatomical defect, consisting of hydrocephalus, Arnold-Chiari malformation and associated meningomyelocele was much the same, 2 being associated with super-imposed pyogenic infection. The fifth case showed hydrocephalus only, of unknown aetiology. The clinical features were of vomiting, lethargy and flaccid paralysis.

The age at death varied from 6 weeks to 2 months, except the case of hydrocephalus only, who survived for 15 months.

3. Abnormalities of the abdominal viscera

Two cases fell into this subgroup

Case 217, a male infant, died at the age of one month from post-operative complications of an operation for congenital pyloric stenosis.

Case 137, a male mongol infant, died at the age of 2 months after a history of the development of jaundice which gradually deepened. Death was due to hepatic failure due to atresia of the bile ducts.

4. Summary of congenital defects

In most of these cases of congenital abnormality death occurred at an early age, 12 out of 16 dying within the first 4 months of life, only 3 surviving more than one year. In most cases signs and symptoms of the anomaly had been present since birth, sometimes with a more acute terminal episode lasting a few days. In 2 cases of cardiac involvement (out of 9) and in one case (out of 5) of central nervous system defect the condition was not suspected until the terminal stages. Eleven out of the total of 16 cases (69%) occurred in male infants, this sex preponderance being particularly noticeable in the cardiac abnormality subgroup, 77% being in male infants. Owing to the short course of the disease in general, no seasonal incidence could be expected. The morbid anatomical picture varied according to the primary cause of death. Histological examination was not carried out frequently in these cases, in the 4 cardiac defect cases in which the lungs were examined microscopically, 2 showed infiltration with

mononuclear cells (in one instance these were conspicuously pigmented), one showed a mixture of polymorph and mononuclear pneumonia, the fourth case showed a frank broncho-pneumonia.

E. ACCIDENTAL DEATHS

The final 2 cases in the seriously ill group of infants died accidentally.

Case 144. A male infant aged 17 months died in coma 14 hours after the ingestion of 75-100 aspirin tablets. Autopsy showed only general congestion and cerebral oedema.

Case 27. A female infant aged 19 months was involved in a road traffic accident and died 12 hours later from multiple fractures of the skull and gross cerebral contusion.

CHAPTER 3

SUDDEN OR UNEXPECTED DEATH IN INFANCY

"And when I rose in the morning to give my child suck, behold, it was dead".

1 Kings, III, 21

PREAMBLE

The third group into which this series of infant deaths has been divided comprised 83 cases (33.2% of the series) in which death occurred suddenly or unexpectedly. Most of these concerned children who were previously in good health or who had only minor symptoms which did not give rise to any anxiety on the part of the parents or, in some cases, medical officers called in to see the child. A small group (15 cases) with an acute, brief history of a few hours are included here as the shortness of the illness led to unexpected death. In two cases a congenital defect had been noted previously (one a mongol, one a cardiac abnormality), but as these conditions did not appear to have given rise to any disability or symptoms and the infants were found dead in bed, they have been included here rather than in the seriously-ill group discussed in Chapter 2.

PART 1. PRELIMINARY CLASSIFICATION

Clinically these cases can be divided into five main groups:

1. Infants who were found dead, or were seen to die, there being obvious evidence of trauma of some kind; all these can be regarded as accidental deaths. This group consisted of seven cases (8.4%), death being due to:

   a. Drowning

   b. Electrocution

   c. Gun-shot wounds

   d. Suffocation due to inhalation of a sweet

   e. Strangulation due to:

      (1) Pram straps

      (2) Electric light switch cord

f. Multiple injuries due to fall from a height.

2. Infants who were found dead, but with no evidence of trauma, and in whom there had been no previous symptoms to indicate that anything was amiss. This group consisted of 25 cases (30.1%).

3. Infants who were found dead, but had previous mild symptoms which did not arouse alarm. 31 cases (37.3%) fell into this group. The symptoms complained of were:

a.	Recent upper respiratory tract infection	16
b.	Feverishness with fretfulness	4
c.	Diarrhoea and/or vomiting	8
d.	Recent exanthematous disease	2
e.	Earache	1

In twelve of these 31 cases, the mother had consulted a doctor who had found nothing of note on physical examination and who did not consider the case of any severity.

4. Infants who died in the presence of an adult. There were five cases in this group (6%). Three died suddenly in their mothers' arms, all had previous mild upper respiratory symptoms; one died while being examined by a doctor, again this infant had apparently trivial symptoms previously, and one died on the operating table. This latter case is included here, not in the accidental death group, as considerable pathological changes were found at post-mortem examination.

5. Infants who died after a brief history (six hours or less) of acute illness, being previously in good health or with only minor symptoms. These are fulminant cases which are included here rather than in Chapter 2 (the seriously ill group) because of the extreme shortness of the acutely ill phase. There were 15 cases (18%) in this group.

PART 2. THE MORBID ANATOMICAL PICTURE, IN BRIEF

Macroscopically at autopsy the cause of death was ascribed to:

1. Asphyxial signs only.
2. Asphyxial signs accompanied by the presence of inhaled vomitus in the respiratory tree.
3. Signs of pneumonia
4. Signs of meningitis.
5. Congenital conditions of a major nature.
6. Emaciation
7. Trauma and
8. No apparent cause.

These can be subdivided according to the five major clinical presentations as in Table XVI

	Accidental death	No previous symptoms	Previous minor symptoms	Death in presence of an adult	Brief acute history	TOTALS
Asphyxial signs only	-	7(4)	10(6)	1(0)	1(1)	19(11)
Asphyxia with inhaled vomitus	-	8(4)	6(5)	1(1)	1(1)	16(11)
Pneumonia	-	9(7)	12(9)	2(2)	11(10)	34(28)
Meningitis	-	-	1(1)	-	-	1(1)
Major congenital defects	-	1(0)	2(1)	1(1)	-	4(2)
Emaciation	-	-	-	-	1(0)	1(0)
Trauma	7(1)	-	-	-	-	7(1)
No apparent cause	-	1(1)	-	-	-	1(1)
TOTALS	7(1)	26(16)	31(22)	5(4)	14(12)	83(55)

Table XVI. Clinical and macroscopic morbid anatomy groups

(Note: Histological examination was carried out in 55 of these cases as shown in parenthesis).

PART 3. THE PATHOLOGICAL PICTURE IN MORE DETAIL, WITH ILLUSTRATIVE MICROPHOTOGRAPHS

The important subgroups from the point of view of the cause of death are those with asphyxial signs (with or without inhaled vomitus), the cases diagnosed macroscopically as pneumonia and the case with no obvious naked-eye pathological change. Histological material was available from these subgroups in 51 instances out of 70 (some 74%), material being now available for illustration in 40 cases. Material was also examined from 4 cases in other categories.

The pertinent clinical and pathological findings, including results of histological examination where undertaken, of the whole group of 83 cases in this Chapter are included in Appendix C.

A brief summary from the 55 cases in which histological (and sometimes bacteriological) material was examined, follows:

1. Infants in whom autopsy showed signs of asphyxia only (apart from minor non-contributory findings).

A. Cases with no previous symptoms

Case No	Figure(s)	Opinion
250	1 - 2	Interstitial and mononuclear pneumonia.
106	3 - 5	Interstitial and mononuclear pneumonia
205	6 - 8	Acute tracheitis and early broncho-pneumonia. Liver changes suggest septicaemia
152	9	Interstitial and mononuclear pneumonia.

B. Cases with previous mild symptoms

Case No	Figure(s)	Opinion
75	10 - 12	Interstitial and mononuclear pneumonia
251	13 - 16	Pneumonia, predominantly interstitial, with early renal infection and myocardial fibrosis(no cardiac abnormality was found otherwise).
91	Slides not available. Mononuclear pneumonia.	
30	17 - 18	Mononuclear pneumonia, predominantly interstitial
174	19 - 21	Mononuclear pneumonia
199	22 - 25	Acute tracheo-bronchitis with early mononuclear pneumonia (gram positive organisms in sections).

C. Cases with a brief acute history

Case No	Figure(s)	Opinion
226	26 - 27	Acute interstitial pneumonia

2. Infants in whom autopsy showed evidence of asphyxia accompanied by the presence of considerable quantities of vomitus in the respiratory tree.

A. Cases with no previous symptoms

Case No	Figure(s)	Opinion
155	28 - 31	Bronchiolitis and early mononuclear pneumonia (Gram positive organisms morphologically resembling Str. pneumoniae in sections)
139	32 - 34	Acute bronchitis and pneumonia, mainly interstitial (incidental finding, cysts of ovary).
140	35 - 36	Acute interstitial pneumonia (Gram positive organisms in section)

Cases with no previous symptoms (cont.)

Case No	Figure(s)	Opinion
17	37 - 39	Mononuclear pneumonia, mainly interstitial.

B. Cases with previous mild symptoms

Case No	Figure(s)	Opinion
1	40 - 41	Mononuclear pneumonia,mainly interstitial
83	42 - 45	Pneumonia, predominantly mononuclear.
159	46 - 47	Early mononuclear pneumonia and enteritis (Gram negative bacilli in section).
59	48 - 52	Pneumonia, bronchial and mononuclear.
120	53 - 56	Acute tracheo-bronchitis and commencing pneumonia.

C. A case dying in the presence of an adult

Case No	Figure(s)	Opinion
103	57 - 66	Acute broncho-pneumonia and mononuclear pneumonia with fibrinous pleurisy.

D. A case dying after a brief acute history

Case No	Figure(s)	Opinion
171	67 - 70	Bronchitis and pneumonia, with hyaline membrane formation.

3. Infants in whom autopsy showed macroscopic evidence of pneumonia or upper respiratory tract infection

A. Cases with no previous symptoms

Case No	Figure(s)	Opinion
33	71 - 73	Fulminant pneumonia (Gram positive cocci in section)
127	74 - 76	Bronchitis and early mononuclear pneumonia (mixed growth of Friedlander's bacilli and Esch. coli from lung swabs).

Cases with no previous symptoms (cont.)

Case No	Figure(s)	Opinion
115	77 - 80	Broncho-pneumonia with areas mononuclear in type (Marasmic infant, scattered Gram positive diplococci in section)
203	81 - 82	Acute tracheo-bronchitis and pneumonia (Str. pneumoniae cultured from tracheal exudate)
57	83 - 85	Interstitial and mononuclear pneumonia.
215	(Slides not available)	Broncho-pneumonia.
246	86 - 87	Tonsillitis, acute cervical lymphadenitis and early pulmonary infection.

B. Cases with previous mild symptoms

Case No	Figure(s)	Opinion
16	88 - 90	Acute broncho-pneumonia
153	91 - 93	Acute mononuclear pneumonia with adrenal haemorrhage and fibrinous pleurisy (Gram negative organisms resembling Friedlander's bacillus in sections).
164	94 - 96	Acute tracheo-bronchitis and mononuclear pneumonia.
210	97 - 99	Acute pneumonia, mainly interstitial
252	100 - 103	Tracheo-bronchitis and pneumonia (Brain cysts present, interpreted as being the sequel of cerebral birth injury).
60	104	Bronchiolitis and early pneumonia (Staphylococcus pyogenes cultured from lung swab and Gram positive organisms in sections)

Cases with previous mild symptoms (cont.)

Case No	Figure(s)	Opinion
61	(Slides not available)	Acute broncho-pneumonia and otitis media (Staphylococcus aureus isolated from lung swab and, together with a coliform bacillus, from pus from respiratory tree).
220	(Slides not available)	Broncho-pneumonia, haemorrhagic adrenal glands. (Heavy growth of a beta-haemolytic streptococcus from respiratory tree).
132	105 - 107	Acute bronchitis, bronchiolitis and early broncho-pneumonia (Swabs from main bronchi yielded growth of Staphylococcus aureus).

C. Cases dying in the presence of an adult

Case No	Figure(s)	Opinion
114	108 - 110	Acute broncho-pneumonia and mononuclear pneumonia with pleural effusion (Swabs from the main bronchi yielded a growth of a penicillin-resistant Friedlander's bacillus).
238	111 - 113	Interstitial pneumonia; incidental finding, left congenital hydronephrosis (Mixed growth of a Friedlander's bacillus and Str.viridans from bronchial swabs)

D. Cases dying after a brief acute history

Case No	Figure(s)	Opinion
161	(Slides not available)	Interstitial pneumonia and

Cases dying after a brief acute history (Case No 161 cont.)

Case No	Figure(s)	Opinion
		enteritis. (Gram positive diplococci in sections)
167	(Slides no longer adequate for photography)	Interstitial pneumonia (Gram positive cocci in sections)
348	114 - 115	Acute interstitial pneumonia.
118	116 - 119	Haemorrhagic pneumonia (Unidentified Gram positive bacilli isolated from lungs)
12	120 - 122	Pneumonia, predominantly mononuclear.
105	(Slides not available)	Mononuclear pneumonia (Gram positive cocci in sections)
182	(Slides not available)	Early mononuclear pneumonia.
206	(Slides not available)	Acute broncho-pneumonia, lung abscess and fibrinous pleurisy. (Gram positive cocci in sections)
229	123 - 124	Pneumonia, mainly mononuclear
39	125 - 126	Interstitial pneumonia.

4. An infant in whom autopsy showed signs of meningitis

A. Previous mild symptoms

Case No	Figure(s)	Opinion
58	(Slides not available)	Acute encephalo-meningitis.

5. Infants who at autopsy showed congenital conditions of a major nature

A. A case with previous mild symptoms

Case No	Figure(s)	Opinion
67	127 - 129	Acute pneumonia; Mongolism.

B. A case dying in the presence of an adult

Case No	Figure(s)	Opinion
19	130 - 132	Tracheo-bronchitis and mononuclear

A case dying in the presence of an adult (Case No 19 cont)

Case No	Figure(s)	Opinion
		pneumonia. Obscure cerebral condition, possibly congenital.

6. No histological material in the one case in this sub group.

7. An infant who died from accidental causes (Strangulation by pram straps).

Case No	Figure(s)	Opinion
5	133 - 134	Lungs showed mild inflammatory changes.

8. An infant found dead, no previous symptoms, in whom autopsy disclosed no apparent cause of death

Case No	Figure(s)	Opinion
213	135 - 137	Probably fulminant septicaemia.

PART 4. EPIDEMIOLOGICAL AND SOCIAL DATA

1. The overall sex incidence in the 83 cases was 51 males and 32 females, but breakdown into the various clinical or pathological subgroups does not show sufficient numbers to indicate a significant sex preponderance in any one.

2. Little information was sought concerning the social circumstances in individual cases, the main data available is the rank of the father. Figures from the statistical centre show that the number of children below the age of two years calculated yearly over a period of five years was, in officers' families 1525, in other rank families 10,105, a ratio of 1:4.7. The deaths of infants from sudden or unexpected causes in the period was three from officers' families, 80 from other rank families, giving a ratio of 1:26.6. This would appear to be clearly significant in comparison with the numbers at risk.

3. Excluding the accidental deaths, 45 of the sudden or unexpected deaths occurred in the October - March period, 31 in the April - September period.

4. The age incidence has been plotted in Figure T1, showing a curve for those dying from "asphyxia", one for those dying from "infective conditions" (pneumonia, meningitis and septicaemia) and one for the total of these two categories. The curves are very similar and show the peak

incidence to be from the second to the fifth months of life.

5. Time of death. In 50 infants found dead, with or without previous mild symptoms, 38 were discovered in the morning when the parents awoke, 12 were found at other times during the day when the infant had been left unattended for some hours.

6. The position of infants found dead was only recorded on a few occasions, but correlation between the position and the histological picture is of considerable value concerning the possibility of mechanical suffocation. Some illustrative cases follow:

a. Found dead in cots, face down or under bedclothes

Case	Position	Histological opinion	Figure(s)
152	Face down on soft pillow	Interstitial mononuclear pneumonia	9
251	Face down: no pillow	Pneumonia, predominantly interstitial with early renal infection and myocardial fibrosis.	13-16
140	Under twin	Acute interstitial pneumonia	35-36
91	Face down in bed-clothes	Mononuclear pneumonia	-
59	Face down	Broncho-pneumonia and mononuclear pneumonia	48-52
203	Under bedclothes	Acute tracheo-bronchitis and pneumonia	81-82
16	Face down in bed-clothes	Acute broncho-pneumonia	88-90

b. Found dead in bed with others

30	-	Mononuclear pneumonia, mainly interstitial	17-18
199	-	Acute tracheo-bronchitis and early mononuclear pneumonia	22-25

c. NOT face down nor under bedclothes

Case	Position	Histological opinion	Figure(s)
205	Lying on back	Acute tracheo-bronchitis and early broncho-pneumonia	6-8
120	Lying on back	Acute tracheo-bronchitis and mononuclear pneumonia	53-56
33	Lying on right side	Fulminant pneumonia	71-73
57	Lying on left side	Broncho-pneumonia	83-85
60	Lying on back	Bronchiolitis and early pneumonia	104

7. In all but two cases, the infants appeared to be well-nourished and cared for. The exceptions were:

Case 115, a male aged four months who was born prematurely (birth weight 3lb 4ozs), but was discharged from hospital in good general condition, weight 5 lbs 15 ozs, at the age of six weeks. At home the infant did not thrive and was found dead one morning, no special symptoms were noticed by the parents beforehand. At autopsy weight was 5 lbs 5ozs, nourishment was poor with wrinkled skin and practically no subcutaneous fat was present. Death was due to broncho-pneumonia in a marasmic infant.

Case 244. This infant was discharged from hospital one week after birth, apparently thriving. According to the parents the child was lethargic one morning, but on admission to hospital was moribund and emaciated. Autopsy revealed no pathological change beyond emaciation with a leathery skin and no subcutaneous fat. No histological examination was performed and death was ascribed to inanition due to emaciation, the only case in this series in which the final diagnosis was completely inconclusive.

PART 5. INTERPRETATION OF FINDINGS

This Part concerns my interpretation of the findings in this particular series; a discussion on the subject of sudden or unexpected death in infancy, based on many series and on professional articles, will follow in Chapter 4.

The interpretation of the histological findings in the lungs in cases of this nature depends to a certain extent on the pathologist concerned and in cases with comparatively minor changes the diagnosis of an infective process could well be questioned. The histological picture in all cases in which material is now available has been reproduced in the series of microphotographs (Figures 1 - 137) to show the degree of pulmonary involvement commonly found. In a considerable proportion these changes were marked, and it is considered that the inflammatory infiltration of trachea, bronchi and/or alveoli to the extent shown, for example in figures 6-7, 13-14, 23, 32-33, 52, 63-65, 81, 86, 101, 105 and 108, would be accepted by any pathologist, whatever his opinion as to the cause of 'cot' deaths, as indicating severe pulmonary infection.

A personal review and assessment of the histological evidence of pulmonary pathology is given in Table XVIII.

	No of Cases	Histological degree of pulmonary involvement			
		Marked	Mode-rate	Significant (Marked + moderate)	Slight
Clinical groups					
A No previous symptoms	15	8	5	13	2
B Previous mild symptoms	20	13	6	19	1
C Died in presence of adult	3	3	0	3	0
D Brief acute history	12	3	8	11	1
TOTALS	50	27	19	46	4

	No of Cases	Histological degree of pulmonary involvement			
		Marked	Moderate	Significant (Marked + moderate)	Slight
Macroscopic Pathological groups					
A Asphyxia	11	7	3	10	1
B Asphyxia with inhaled vomitus	11	7	2	9	2
C Pneumonia	28	13	14	27	1
TOTALS	50	27	19	46	4

Table XVIII Degree of pulmonary involvement found histologically in sudden or unexpected death in infancy, analysed according to major clinical or macroscopic pathological groups

Excluding death from firm cases (meningitis, congenital defect and trauma), 50 cases were so analysed and in summary the findings are:

Marked pulmonary changes 27)
) significant in 46 (92%)
Moderate pulmonary changes 19)

Slight pulmonary changes 4

Review of the clinical picture, final pathological diagnosis and ancillary data enables certain general conclusions to be drawn from this series:

1. Sudden or unexpected death in infancy can result from a number of causes. A minority are due to well-defined pathological processes. In this series of 76 cases (the seven traumatic cases being excluded) a major congenital defect was the cause of death in four, and meningitis in one. The remainder were 'cot' deaths (56) or fulminant cases (15).

2. A considerable proportion of sudden or unexpected deaths in infancy can be ascribed, in my opinion, unequivocally to acute infective processes, generally pulmonary. Marked evidence of pulmonary infection was seen in 54% of cases examined histologically, moderate changes of this nature were described in a further 38%, in only 8% were histological changes considered to be slight. A proportion of cases showed advanced changes including pleurisy and lung abscess.

3. Infants may have post-mortem evidence of severe pulmonary infection, yet show little or no evidence of this clinically before death. Of the 50 cases in this series examined microscopically and found to have significant evidence of pulmonary infection, 29.4% had no previous history of illness and 41.9% had only minor symptoms which did not give rise to any anxiety. Thus in 71.3% the death was completely sudden or unexpected.

4. Pulmonary infection in infancy may be fatal within a very short time of its apparent commencement. The series of 15 cases in this Chapter who had a brief acute illness are included here to illustrate the extreme rapidity with which illness in an infant can prove fatal. Two cases are cited to emphasise this point.

a. An infant aged two months (Case 118, Appendix C, 3D) was put to bed after an evening feed, apparently in normal health. At 1 a.m the mother noticed that the infant's breathing was extremely rapid, her colour was grey and there was profuse sweating. A medical officer, summoned immediately, diagnosed acute bronchitis, but the child died before transport to hospital could be arranged. Autopsy showed a haemorrhagic pneumonia (Figures 116-119). Had the mother not awakened, the child would have been found dead next morning, another 'cot' death.

b. A male infant aged seven months (Case 206, Appendix C, 3D) was examined by a medical officer on the evening of 21 November 1959, and a diagnosis of mild bronchitis was made. No anxiety was felt.

The baby appeared to be better next day until 8 p.m. when the mother noticed he was unresponsive. Seen by a medical officer half an hour later, the infant was found to be extremely ill with cyanosis, a respiratory rate of 50 per minute and pulse rate 180 per minute. Numerous rhonci and râles were heard over the lungs and there were signs of meningism. The child died less than an hour later. Autopsy revealed widespread consolidation of the lungs with an abscess cavity in one lung, and a fibrinous pleurisy.

5. <u>As a collorary to the above, the rapidity with which fatal illness may arise in infants can lead to death without the parents or other responsible persons being aware that anything was amiss with the child</u>.

Of the 56 cases of sudden or unexpected death in which previous symptoms were mild or absent, 50 were found dead, generally in the morning when the parents awoke (38), or at other times of the day when the infant had been left unattended for some hours (12). In these instances a brief acute illness, as occurred in the remaining 15 cases, could well have occurred during the night or while unattended during the day and been unnoticed by the parents, the child being found dead when last seen some hours previously. This "appalling swiftness with which death in the form of natural disease snatches young life" (Bowden 1950) is considered to be a most important factor in the interpretation of the cause of sudden or unexpected death in infancy.

6. <u>A history of recent minor symptoms does not appear to be of significance</u>. Analysis of the 26 cases in which a baby was found dead, with no previous symptoms noted by the parents, shows almost the same picture as regards histological involvement of the lungs as in the 30 cases with previous mild symptoms.

Four regimental medical officers (whose assistance is gratefully

acknowledged) co-operated in an enquiry into minor complaints in infancy. On domiciliary visits where there were infants under the age of two years, who had not been seen by a doctor recently (and who were not the reason for the visit), the mother was asked "Is the baby well?". In four cases out of a total of 45 investigated, the mothers volunteered the information that the infants had some symptoms. In the remaining 41 instances in which the mother said "Yes, the baby is well", a detailed questionnaire concerning symptoms was made. In 16 cases such direct questioning revealed some symptoms (respiratory in seven, skin complaints in three, alimentary in three and general symptoms in three), so that overall 44% of these infants did appear to have minor complaints though this was originally denied when asked a casual question. This figure is slightly lower than the admitted symptoms in 54% of cases of sudden or unexpected death, but it does indicate that minor symptoms are of common occurrence in the infant population at large.

7. Cases in which the circumstances could suggest external occlusion of the nose and mouth all showed marked histological changes in the lungs. Data is incomplete concerning the position of the infant when found dead, but in all the cases enumerated in para 6(a) and (b) of Part 4 (page 62) where mechanical suffocation was theoretically a possibility, widespread histological changes were found in the lungs, and the picture did not appear different to that seen in a small proportion of cases (6(c)) where a positive statement was recorded that the infant's airway was free from interference by pillows or bedclothes.

8. In a proportion of cases some evidence of a bacteriological cause was found. Systematic bacteriological studies were not made as a routine by some pathologists on the material obtained at autopsy, but in eleven cases sections of lung tissue stained by Gram's method showed organisms, Gram positive in nine. Nine cases gave a growth of potential pathogenic

organisms identified as a Streptococcus pneumonia in two, a Staphylococcus aureus in three, a Freidlander's bacillus in three and a beta-haemolytic streptococcus in one. One additional case gave a large Gram positive bacillus on culture which was not identified, but the original anxiety that this could be a strain of Bacillus anthracis was not substantiated.

Although negative findings were not recorded, so that we cannot tell in what proportion of cases these studies were carried out, the finding of positive cultures of these organisms is deemed of significance.

9. In a small number of cases in which the infant's serum proteins were studied, there was no evidence of a hypogammaglobinaemia. An article by Spain et al (1954) suggesting that hypogammaglobinaemia might underlie sudden or unexpected death in infancy did not come to my notice until late in this investigation. Electrophoretic study of the serum proteins in four cases were carried out and subsequently on a series of cases in the Far East (not included in this analysis); all showed a normal pattern.

10. In the vast majority of cases there was no evidence of interference with nutrition or other signs indicating improper care of the infants.

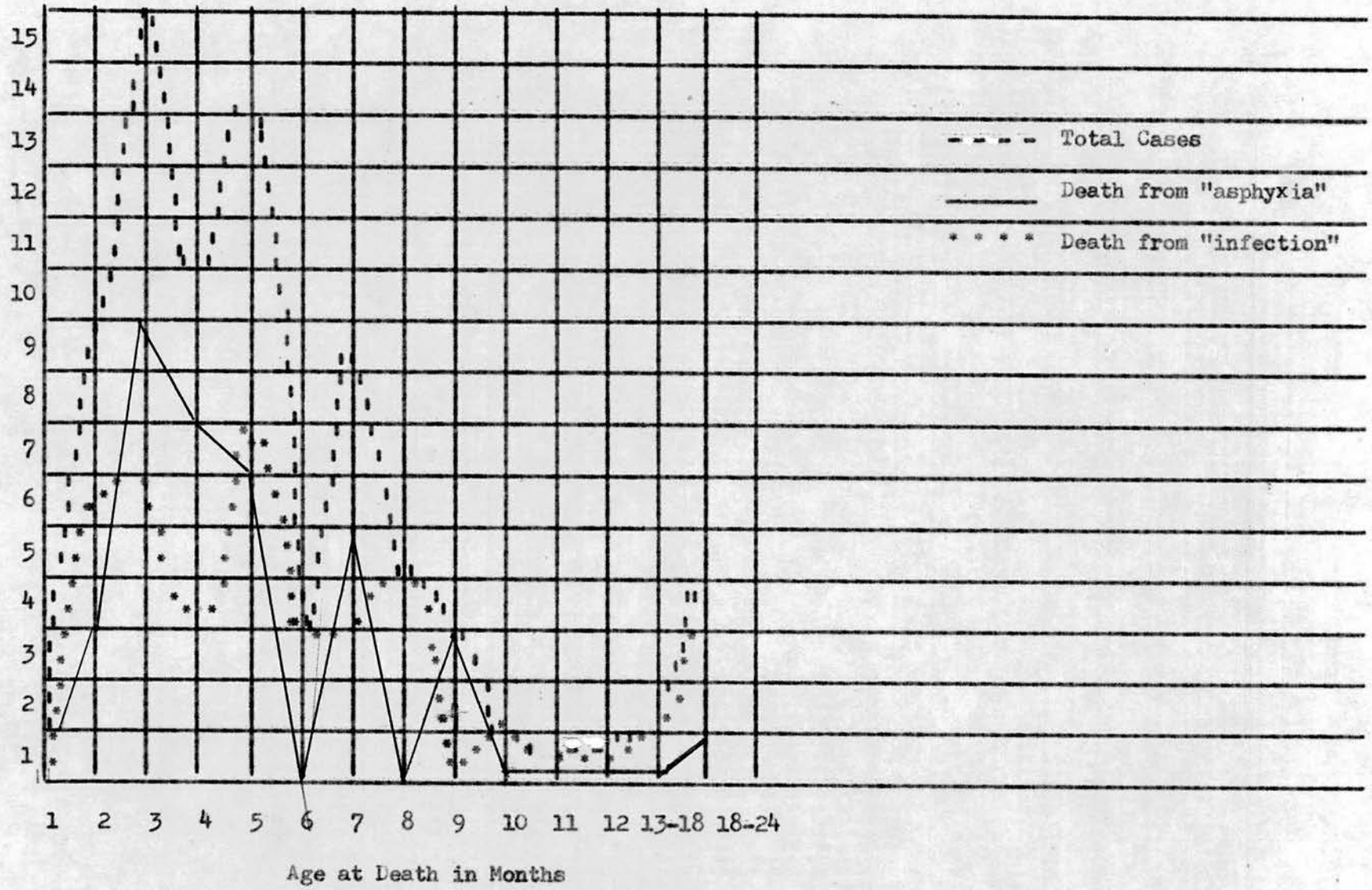

Figure T.1. Age incidence in 71 cases of sudden or unexpected death in infancy.

CHAPTER 4

DISCUSSION ON SUDDEN OR UNEXPECTED DEATH IN INFANCY

"And this woman's child died in the night; because she overlaid it"

(1 Kings, Chapter III, verse 19)

PART I. LITERATURE REVIEW

Scriptural warrant for the diagnosis of accidental suffocation of infants found dead in bed appears to be implied by this quotation from The Book of Kings, and indeed it would appear that this diagnosis was usually accepted until late in the 19th century as the cause of sudden death in infancy, with the implication that a certain number of cases were deliberate infanticide.

Howard (1960) quoted revealing statistics from last century on the quality of medical care in infancy and the attitude often adopted towards infant deaths. Of 297 deaths in children in a Manchester district in one quarter of 1846, only 126 had received medical attention during life and many of these were already in extremis, medical aid only being called to obtain a medical certificate of death to facilitate registration and disposal of the body. Only 187 inquests, on all ages, were held in that period in the whole of Manchester and Howard quoted the evidence of a surgeon to a Royal Commission in 1845 that "sudden death in infants is too common a circumstance to be brought before the attention of the Coroner". Indeed, he continued, the justices of the peace at that time often obstructed the Coroner's duties by refusing their expenses on the grounds that certain inquests were unnecessary, the Chief Constable of the East Riding of Yorkshire in 1847 directing the police that "the Coroner should not be called or informed in cases of mere accidental death such as ..... infants overlaid in bed".

In a fascinating paper giving revealing sidelights on sociological problems in those days, read before the Edinburgh Medico-Chirurgical Society in June 1892, Templeman reported that in Dundee during the period 1882 - 1891, 399 cases of infants found dead in bed with their parents were reported to the police. He personally had examined 256 of these cases; many of his findings hold good today. The risk to infants was greatest in early life, there being a constant risk for the first 3 months, the hazard then rapidly decreasing. 62% of the cases occurred in the winter months, October to March. The usual history was that a child would be put to bed, apparently in good health, the mother often fed the baby (at that period breast-feeding was almost universal, certainly among the poorer classes), then fell asleep and found the baby dead next morning.

External examination of the infants was mainly negative, there were no marks of violence and as a rule no flattening of the nose or face from pressure. Post-mortem lividity developed early, being pronounced on the side on which the infant was lying. The eyes were slightly congested, the lips livid, the tongue did not protrude. Frothy mucus, often blood-stained, was noted about the mouth and nostrils. In the majority of cases permission for post-mortem examination was not given. Where autopsy was carried out, the findings were those of death from asphyxia - congested cerebral membranes, engorgement of the internal organs especially the lungs, kidneys and large thoracic veins; the blood was fluid and dark, the right side of the heart distended, the left contracted and empty. In about half the cases "punciform" subpleural and subpericardial haemorrhages were noted and the larynx, trachea and bronchi were congested, containing frothy, often blood-stained, mucus.

Apart from the addition of special examinations, particularly histological, the history and autopsy findings are those described by many authors (cited later) and in the present series of cases. The interpretation

by Templeman, however, was that all these cases were instances of mechanical suffocation and ascribed to the ignorance and carelessness of mothers, drunkedness, overcrowding, illegitimacy and the insurance of infants, the latter leading to such temptation that "some parents sacrificed their childrens' lives by neglect if not by more direct and speedy measures". Whilst Templeman himself did not consider that the high infant mortality rate had any criminal connection with insurance, it had been redorded earlier (Select Committee Report, 1854, cited by Howard, 1960), that child murder for the sake of burial money prevailed to a "frightful extent".

Two cases illustrated by Templeman are of particular interest. In one, the mother of a 4 month old healthy infant put the child to breast, covered the baby's head with a shawl as the night was chilly, walked 300 yards and on arrival at her destination found that the baby was dead. In the second case, a mother was talking to friends whilst feeding the baby, on withdrawing it from the breast 5 minutes later the infant was found to be dead. In both these cases there were the usual appearances of death from asphyxia, but in neither was there any question of external mechanical suffocation and both babies were breast-fed.

The author suggested that the only safeguard against these fatalities be that the child should occupy a separate cot and he quoted a German law to the effect that children under the age of 2 years must not sleep in the same bed as parents or nurses. It is a pity that his premise, that these deaths were all due to overlaying, is not borne out by present day experience; in general infants nowadays occupy separate cots, but the problem of sudden or unexpected death in infancy is still with us.

The section on Sudden Deaths in Infants in "La Mort et la Mort Subite" (Brouardel, 1895) appears largely to have escaped the notice of authors of this century. (It is quoted, however, by Camps, 1963). Brouardel listed

5 principal causes of sudden death in infancy as:

1. Syncope, generally due to a cardiac condition.

2. Convulsions, due to such diverse causes as congenital syphilis, meningeal haemorrhage (often associated with teething), fevers and intestinal upset.

3. Asphyxia, mainly due to laryngeal spasm caused by irritation, laryngitis or laryngo-bronchitis. The author stated that such spasm occurs particularly between the hours of 10 pm and 4 am, it can follow minor inflammation of the laryngeal mucosa yet, though the spasm can cause fatal asphyxia, no obstruction to the trachea or larynx is found at autopsy. He also indicts enlarged thymus glands as a possible cause of death.

4. Pulmonary congestion. Bronchitis is a frequent cause of death in children aged 5 to 6 months; often when such a child is found dead, suffocation is suspected, but Brouardel stresses that capillary bronchitis or "Laennac's suffocating catarrh of infants" can cause intense pulmonary congestion which can be rapidly fatal. Autopsy findings are described as subpleural petechiae, firm lungs which when squeezed show beads of mucopus being expressed from the smaller bronchi of the cut surface, and areas of atalectasis.

5. Abdominal catastrophes, infantile cholera and haemorrhages. Brouardel stresses that the pathogenesis of sudden death in infancy is different from that in adults as the former develop congestion and severe reactions to nervous stimuli with ease.

In 1915, Brend published an Enquiry into the statistics of death from violence and unnatural causes and discussed infant deaths in Part III of his report. In particular, he dealt with statistics relating to death ascribed to mechanical suffocation, including overlaying. He quoted a Home Office figure of 1173 deaths in children (ages not stated) from suffocation

in England and Wales in 1912. He considered that there was a case for believing that a considerable proportion of these cases were, in actual fact, deaths from natural causes. He analysed population densities in urban and rural areas in relation to mortality rates and concluded that overcrowding was not a significant factor. In drawing attention to the fact that coroners accepted a verdict of death from overlaying without an autopsy, he pointed out that signs of an asphyxial death can be indistinguishable from the signs seen in deaths from such causes as rickety convulsions and "debility". Even in cases of broncho-pneumonia, patches of consolidation could be overlooked by a general practitioner and parents may have failed to notice that the child was ill for a day or two, or regarded any symptoms as trivial and due to a "cold". Death from "mechanical suffocation" showed a marked seasonal variation, exactly parallel with mortality from broncho-pneumonia, convulsions and "debility". (In this connection, see the more modern correlation of sudden death in infancy with respiratory disease in families discussed by Sutton and Emery (1966), referred to on page 92). Of 134 inquests on children under the age of one year in the South-Western and Westminster Coroner's districts in London, only one verdict of suffocation in bed with others was passed, whereas in other Coroners' districts as many as 29% of cases had such a verdict recorded. This was interpreted by Brend as being due to the fact that some Coroners had an expert carrying out post-mortem examinations and in these circumstances few cases were ascribed to overlaying. A very important sociological aspect is his comment that "it is an extremely cruel thing to leave a mother with the lifelong impression that she herself killed the infant unless there is the clearest evidence of the fact". He finally noted that in France, where all autopsies were carried out by expert pathologists, deaths from overlaying were rare, 36 being recorded in Paris in 1911 from a total population of nearly 3 million people.

Farber (1934) described fulminating streptococceal infection as a cause of sudden death in infancy. He described a typical case of this nature - a 3-month old baby was fed at 2o'clock, it seemed well, but was found dead, lying on its back, one and a half hours later. The diagnosis made was "suffocation". Histologically the lungs showed very early interstitial infiltration of the alveolar walls and peribronchial regions, a pure culture of a streptococcus haemolyticus was obtained from the heart blood and the lungs. He considered that such an infective process was not primarily pulmonary, but a widespread involvement of the body following bacteraemia. Though early interstitial infiltration of the lungs was almost constant, no physical signs appeared as death occurred before appreciable pulmonary involvement had time to develop. The author mentioned that there was a popular misconception as to the normal size of the thymus gland and, while admitting that a "thymic" death was an easy way out of a distressing condition, stated that no thymus gland was regarded as being pathological in size in a series of 2000 autopsies performed at the Children's Hospital in Boston, USA. Farber stressed that fulminating streptococcal infection was but one of the causes of sudden death in infancy and did not imply that all cases could be explained in this way. He concluded that a diagnosis of suffocation in early life should not be accepted unless a complete port-mortem examination had been carried out.

In a further paper (Farber, 1938) he considered that, if accidents were excluded, virtually all cases of unexpected death in early life fell into the category of "death from natural causes".

Gafafer (1936) reviewed the changes in mortality from cases reported as deaths from mechanical suffocation in infants under the age of one year in different geographical areas of the United States during the period 1925-32. He recorded that, of 2405 infants dying accidentally in 1930, 849 (35%) were attributed to mechanical suffocation; the same percentage

was reported in 1932.

Abramson (1944) also drew attention to the alarming frequency with which accidental mechanical suffocation was judged the cause of death in infancy, quoting a figure of 139 such deaths in a 5-year period in New York.

This attribution of mechanical suffocation as a cause of sudden death in infancy was again questioned by Woolley (1945). He admitted the seriousness of the problem and discussed the evidence upon which this diagnosis was made. He analysed the atmosphere breathed by infants covered with various types of bedding and could find no alteration in oxygen or carbon dioxide content unless the covering included a rubber sheet secured tightly at each corner. He concluded that there could be no question that flimsy bedclothes could be an effective deterrent to free gaseous exchange. Woolley then discussed possible causes of these deaths under the headings of infections, congenital abnormalities and physiological dysfunction. Under the latter heading, he drew attention to the exaggerated pyrexial response seen in seemingly unimportant infections, the rapid deterioration seen in normal fluid and electrolyte balance, the poor tolerance to anaesthesia and surgical procedures and the rapidity with which vitamin deficiency became manifest in infancy as indications of the physiological immaturity or imbalance of the very young, which could be an important factor in sudden death.

Interest in this question now quickened and it was discussed in an editorial in the British Medical Journal (BMJ 1945). This dealt mainly with the paper by Abramson (1944), but it was considered that insufficient data of pathological detail was available. Attention was drawn to a report from New Zealand which gave a figure of 16 cases of accidental mechanical suffocation in a series of 951 infant deaths, the incidence of 1.3% being very much at variance with the 35% quoted by Gafafer (1936). This editorial raised the question of <u>status thymaticus</u> or metal deficiency as

possible factors.

Davidson (1945) quoted figures from Birmingham. Since the passing of the Coroners (Amendment) Act of 1926, coroners had been given the option of waiving an inquest if they so desired, even though a post-mortem examination had been held, and since then all infant deaths in this region suspected of having been caused by suffocation had been examined by autopsy. Of 318 infant deaths in the period 1938-44, 108 occurred in infants in bed with adult, 18 of these were ascribed to mechanical suffocation. Of 210 deaths in cots, the babies being alone, mechanical suffocation was the final diagnosis in 6 instances. The remaining 294 cases (in bed with others or alone in cots) were all shown to have died from natural infection, respiratory infection alone being found in 152 cases and such infection associated with otitis media in a further 77 cases. The majority of these deaths (71%), from whatever cause, occurred in the winter months October to March. The author stressed the importance, so often neglected in the past, of carrying out post-mortem examination as part of the routine investigation of cases of this nature.

From Australia came the same type of reasoning. Bowden (1950) stressed that natural disease can strike with great rapidity in babies with, in fatal cases, little pathological change to be found at autopsy, and the misdiagnosis of mechanical suffocation was frequently made. He quoted a figure of some thirty babies being found death each year in the city of Melbourne, some face downward or under bedclothes, with sometimes considerable cyanosis suggesting suffocation. He posted the question - do babies accidentally suffocate in these circumstances? After discussing the paucity of naked-eye pathological change, the presence of vomitus in the respiratory tree which may be agonal, the fact that infants may be suffering from a fatal illness not discernible to even trained observers and the mobility of an ordinary baby, he concluded that few, if any, of these

deaths were due to suffocation, but resulted from fulminant natural disease.

Bowden and French (1951) extended this work by further epidemiological, histological and bacteriological studies. A significant increase in unexpected deaths in infancy was found in the winter months, May, June and July (this work was carried out in Australia). They disagreed with the belief commonly held that after death there was a fairly rapid invasion of the body by micro-organisms from the intestinal canal and carried out extensive bacteriological studies, including attempts to isolate influenza virus, in 22 cases. In 18 of these, pathogenic or potentially pathogenic organisms were obtained from the lungs, positive isolates also being obtained on occasion from other sites including the heart blood (in 6 cases), the brain (in 3) and the ears (in 3). In 2 cases a Type A influenza virus was isolated. Histologically these cases all showed a similar picture in the lungs, mononuclear cell infiltration, plasma cells predominating, being present in the upper part of the bronchial tree. These authors concluded that the explanation of these sudden deaths was not to be found in mechanical suffocation, but in disease processes which were frequently only discovered by careful investigation. Sudden deaths in infancy were largely a reflection of the prevailing disease in the community at the particular time.

In 1951, Gruenwald and Jacobi described a diffuse mononuclear pneumonia in most cases of sudden or unexpected death in infancy and discussed at length the postulate that these infants had had a viral infection and succumbed before bacterial pneumonia, which was often the sequence in severe pneumonia in older age groups, had supervened. They presented clinical data and pathological findings in 76 infants dying either suddenly or after a brief period of prodomal symptoms. Such symptoms were present in 43 cases (56%), in the majority they comprised upper respiratory tract infections. A much smaller group presented with

diarrhoea and vomiting, an occasional infant had convulsions. Those which were admitted to hospital were acutely ill, in a state of respiratory distress, and died within 12 hours. The great majority however (61 out of the 76 cases) died much more rapidly or suddenly. Even a few hours before death, clinical signs of respiratory involvement were absent. Most of the cases (56) died in the first few months of life. The pathological picture showed little variation. Moderate cyanosis was noted, with frothy fluid often being present in the nose and mouth. There was no excess fluid in the body cavities, petechiae of the epicardium, pleura and thymus were frequently present. The lungs were voluminous, purple-grey in colour; on sectioning the cut surface was red and moist, exuding frothy fluid, the picture grossly resembling pulmonary oedema, but as this exudate contained cells, it was not considered to be purely oedema fluid. Microscopically, the lungs showed areas of marked thickening of the alveolar walls, the alveoli, sometimes atelectatic, contained an exudate with varying numbers of large mononuclear cells. The alveolar walls sometimes showed a cellular infiltrate, mainly of large mononuclear cells and lymphocytes; sometimes there was a superadded broncho-pneumonia with polymorphonuclear cells. The affected areas were interspersed with areas of fairly normal-appearing tissue. The spleen was soft, with conspicuous follicles containing reactive centres. Special stains for bacteria were usually negative, in those cases in which organisms were seen in the lungs, broncho-pneumonia changes (polymorph infiltration) were generally present. The authors suggested that studies of cases of this nature could be hampered by erroneous pathological interpretation, especially the fact that petechial haemorrhages suggested suffocation from external causes and the relatively inconspicuous pulmonary histological changes were then ignored. They drew attention to the fact that such pulmonary changes were found in infants with more protracted disease or who died from other causes and suggested

that the viral infections they postulated as the cause of this mononuclear or interstitial pneumonia were not universally fatal. The possibility of the occurrence of numerous non-fatal cases should receive serious consideration in attempting to discover the cause of unexpected death in infancy.

Swinscow (1951) by statistical analysis, concluded that 'cot' deaths were nearly all due to natural causes. He conceded that mechanical suffocation, when infants were in bed with others or due to aspiration of food, could still occur, but stressed that no infant death should be attributed to accidental mechanical suffocation unless there was clear positive evidence of this.

In a commentary mainly based on Swinscow's paper the British Medical Journal (BMJ 1951) drew attention again to the importance of full autopsy procedures in cases of this nature. The fact that inhalation of milk or stomach contents could be an agonal manifestation in anoxial deaths was also mentioned.

Werne and Garrow (1953a, 1953b) and Garrow and Werne (1953), in a series of papers, discussed findings in 3 groups of infants; (1) those found dead having been apparently in good health (2) those observed to die suddenly (mechanical suffocation from external causes being excluded with certainty) and (3) those dying immediately after unquestioned violence.

In the first group, autopsy showed a definite cause of death (congenital heart disease, meningitis, acute laryngo-tracheo-bronchitis or frank pneumonia) in 16.8%. In the remaining 83.2% the death remained unexplained at the conclusion of the macroscopic autopsy. Thirty-one consecutive cases in this latter group were studied microscopically, in all there were inflammatory lesions in the upper and lower respiratory tract, vascular changes and reactive changes in lymphoid tissue, including that in the spleen. Their interpretation of these changes was that death was

caused by fulminant respiratory disease.

Of 26 cases in the second group, infants dying in the presence of an adult, 9 had gross cardiac disease and one showed a frank pneumonia. The 16 cases without conclusive gross autopsy findings all showed inflammatory lesions of the respiratory tract histologically. These lesions were identical with those seen in infants found dead, offering additional evidence that fulminating respiratory disease is a common cause of sudden, unexpected and apparently unexplained death in infancy.

The third paper dealt with the examination of infants dying immediately after violence (drowning, carbon monoxide poisoning, massive burns, suffocation by live steam and miscellaneous causes, totalling 26 cases in all), local lesions in the respiratory tract were not constant, usually not multiple and when present were of mild degree. The authors pointed out that since respiratory infections are so common in infancy and early childhood, one would expect to see such minor lesions, acute or not, in the respiratory tree of some infants, irrespective of the cause of death. Hyperplastic changes in lymphoid tissue and hyperaemia or haemorrhage of the thymus, lymph nodes and viscera were not found in this third group, in contrast to the picture seen in sudden, unexpected death.

Bowden (1953), whose earlier papers from Australia have already been mentioned, further discussed sudden death in infancy, based on the analysis of 320 cases investigated over a period of 6 years (76 of these did not fall into the categories discussed here, being over the age of 2 years). Approximately half of the number of infants died in the first 6 months of life, 66% in the first year. The majority were found dead in bed and had not received recent medical attention. The pathological causes of death in 287 cases were tabulated, of the 62 causes listed only a few occurred with any frequency. There was evidence of acute respiratory infection in 133 cases (46%), this being the commonest and most outstanding lesion

seen. Bowden stressed that in this 46%, the lesions were considered of sufficient severity to explain the death; minor degrees of bronchitis could be found in "control" cases (dying from accidental causes). Petechial haemorrhages in the heart, lungs and thymus and the picture of an asphyxial death could be conspicuous features although death had resulted from natural disease. Other frequent causes of death were acute myocarditis (8.7%) and meningoccocal septicaemia (7.8%); in all, infective conditions accounting for 85%.

Barrett (1954) discussed recent literature on sudden death in infancy. Most recent authors, he said, had concluded that such deaths were mainly due to fulminating infection, but he questioned the validity of this conclusion by reference to a series of 176 autopsies on infants, which included 51 sudden or unexpected deaths, performed by himself or his colleagues. He made a distinction between true "cot" deaths, babies found dead in bed who had been apparently well when last seen, and death in those with previous symptoms. In the former group, no definite cause of death could be demonstrated in the majority, inflammatory changes in the lungs only being considered of significance in 4 out of 17 cases. Bacteriological studies were unrewarding. Having discussed the various hypotheses put forward, Barrett concluded that only a small proportion of "cot" deaths were due to fulminant infection caused by familiar organisms such as the streptococcus. Some of the others might be infective, possibly viral, some might be due to mechanical suffocation caused by bedclothes or pillows, perhaps the majority were due to the inhalation of regurgitated food into the lung. He appealed for a clear distinction between what he termed practical expediency and scientific accuracy, as the attribution of these deaths to fulminant infection on insufficient grounds, for sociological reasons, might mask the true cause and "so delay the cure of an evil which is too apt to be regarded with complacency".

Legal aspects of sudden death in infancy were discussed by Smith and Fiddes(1955). While attention was drawn to the fact that young infants often die unexpectedly in bed, without marked symptoms, from a number of causes such as acute congestion of the lungs, acute infective gastro-enteritis (without diarrhoea and vomiting) and convulsions, these authors stated that accidental overlaying of children causes quite an appreciable loss of infants annually. An important forensic point mentioned is that in death from overlaying there is evidence of flattening and pallor of the nose and cheeks of the infant, with lividity of the surrounding parts.

Arey and Sotos (1956) analysed a series of 103 cases of unexpected death in infancy (20 were over the age of 2 years). Seventy one had been ill for more than 24 hours, but the symptoms were trivial and the severity of the disease was not appreciated. The leading cause of death (in just over 40%) was infective disease, congenital malformation accounted for some 18%. Of 10 sudden deaths in apparently healthy infants, 6 had bacteriologically proven septicaemic conditions (4 pneumococcal and 2 haemolytic streptococcal); in 4 the cause of death was recorded as inconclusive.

In 1956, Emery and Crowley drew attention to the inadequacy of clinical histories in many cases of sudden death in infancy, illustrating their argument by an analysis of 50 cases in which a detailed history was obtained after police investigations and coroners' inquests were completed. In only 5 cases did the inquest and later histories agree in all essentials, in 35 the later history revealed information directly relating to the cause of death which was not available at the inquest. They suggested that symptoms were usually present previous to "sudden"death, but these were overlooked in the situation evoked by police enquiries and the coroner's inquest to exclude unnatural death. The authors suggested that some cases of illness could be diagnosed and treated and that in unexpected deaths, a

necropsy should be conducted in hospital, after a careful history had been taken, and the coroner only informed if anything but a natural cause of death was found.

Duthie and Goodbody (1957), however, doubted whether a more accurate history would contribute materially to an increase in diagnosis and treatment, pointing out that many children had mild respiratory and gastro-intestinal symptoms, but did not die. They suggested the interview of 50 "control" mothers whose babies did not die (in this connection the results of such interviews in 45 cases are reported on page 68). These workers themselves found that symptoms were absent or minimal in many cases and reported that in nearly one-third of cases of sudden death in infancy no satisfactory cause, histological or bacteriological, could be found.

In 1957 Cruickshank and his colleagues investigated sudden or rapid death in Gurkha infants in Malaya and Hong Kong. Autopsy, including histological examination, was permitted in 19 cases. Eleven of these showed pulmonary changes interpreted as being those of an interstitial mononuclear pneumonia, 8 showed the features of a bacterial pneumonia. As these cases occurred in an Asian community, their discussion included consideration of the possible role of thiamine deficiency, although clinically the condition was not that of the usually accepted syndrome of infantile beri-beri; thiamine levels in a series of infants were carried out, with the following results:

	Serum thiamine levels in mg %	
Group	Range	Average
Accepted normal in UK	14 - 18	
Normal Gurkha infants(8)	5.1 - 18	9.2
Rapid death in Gurkha infants(9)	0 - 19.4	5.1
Non-fatal respiratory disease in Gurkha infants (10)	0 - 20.4	6.7

It was hence suggested that thiamine deficiency may have played an aggravating role in these cases.

A further leader in The British Medical Journal (BMJ, 1957) discussed the problem of sudden death in infancy anew. After quoting a number of authors already cited above (Arey and Sotos (1956), Emery and Crowley (1956) and Barrett (1954)), a further unpublished series of 150 necropsies performed on infants in a British hospital was presented. 45 of these were in infants over the age of 7 days who died within 24 hours of admission to hospital. The majority of cases showed infective features, major in most, minor in 5. The conclusion was that most pathologists would now agree that sudden death in infancy was usually the result of infection, the view also held by most clinicians. However, it was stated that the main cause of "cot" deaths, that is those cases in which infants, apparently well beforehand, were found dead in bed, was as yet undetermined.

This leader prompted Henderson (1957) to write about his view that cot deaths were not due to overwhelming infection, but to mild infections with associated myocarditis and electrical failure leading to cardiac arrest. Such myocarditis may not be demonstrable post-mortem.

Tregillus (1958), however, still considered that in many cases of infant death the obvious explanation was suffocation. In his experience an adequate cause of death, as judged by post-mortem, including histological and bacteriological investigations, was found in only some 25% of cases. He did not consider that occasional mononuclear cells in the lung alveoli of a previously healthy infant was adequate evidence of death from pneumonia. He still considered that mechanical suffocation by overlaying or from soft pillows was possible, and put up a plea for babies always to be nursed in a separate cot with a firm mattress and no pillow.

In reply, however, Davidson (1958) and Emery (1958) both again stressed that in their opinion most cases of sudden death in infancy showed a natural

cause of death if autopsy was performed by a skilled pathologist. Indeed the latter went as far as to suggest "that the normal child is never simply found dead in bed or cot from external mechanical suffocation".

In order to investigate this problem of sudden death in infancy, the Ministry of Health set up a steering committee in 1953. An interim report (Banks 1958) showed that of 64 such cases in London, 38 (73%) were found to have died from tracheo-bronchitis, 11 (21%) from bronchitis or broncho-pneumonia and the remaining 3 from septicaemia or gastro-enteritis. The findings from a group working in Cambridge were not so definite; of 17 cases studied there, 3 died from pneumonia and one from meningococcal septicaemia. In 13 cases the cause of death remained uncertain although 6 of these showed inflammatory changes in the respiratory tract. Cases in both areas were 3 times as prevalent in winter as in summer, the proportion of males to females was 1.9:1; these are features to be expected in death of babies from respiratory infection. Few deaths, however, could be ascribed to demonstrable bacterial infection and the steering committee decided to pursue virological studies.

In 1960, a different theory as to the cause of death in infancy was put forward by Parish and his co-workers, the hypersensitivity to milk hypothesis. It was not completely new as workers in the past had visualised the possibility of milk sensitisation being of importance in this and other conditions. Thus Anderson and Schloss (1923) had shown, in their investigations into infant nutritional disorders, that precipitins to milk proteins could be demonstrated in the sera of some infants and that these antibodies could sensitise guinea pigs passively to anaphylaxis. Clein (1958) had shown that up to 6% of infants during the first few months of life were allergic to cow's milk. Methods of demonstrating antibodies by a sensitive coated tanned red cell technique described by Boyden (1951) were used by Gunther el al (1960) to show that normal infants aged 7 - 97 weeks

often had milk antibodies in their serum, to titres up to 1/1000, with a modal distribution around 1/64. Of 286 sera tested, 4% had a titre of 1/256, 1% had a titre of 1/512 and a single serum a titre of 1/1000. Of these infants 32% were mainly breast-fed until the age of 6 weeks. Barrett (1954), already cited, had concluded that perhaps the majority of sudden deaths in infancy were due to the inhalation of regurgitated food into the lungs. Such inhaled food might not cause death by directly obstructing the air-passages, but an amount of milk too small to cause immediate asphyxia might excite an inflammatory response, accompanied by pulmonary oedema, or the absorption of undue amounts of milk derivations into the blood stream might cause a state of shock.

Parish et al (1960a) carried out experiments on guinea pigs sensitised to cow's milk. Administration of a challenge dose of milk over the glottis into the larynx of unsensitised, conscious guinea pigs was without untoward effect. If, however, a small amount of milk was introduced into the larynx of a sensitised animal, a characteristic anaphylactic reaction followed, often fatal. This reaction, and the pathological findings, were those of anaphylaxis and did not resemble those seen in human cot-deaths. When light anaesthesia was produced in the experimental animals, as a method of simulating the condition of a sleeping child, however, there was a complete absence of the dramatic features of anaphylaxis; instead, very soon after the introduction of the milk preparation into the larynx of the sensitised, anaesthetised animal, it stopped breathing without any sign of a struggle.

In a subsequent paper (Parish et al, 1960b), these workers tried to relate their findings more directly to sudden death in infancy. Sera from cases of "cot" death were examined for the level of milk antibodies and compared with a random selected from infants of comparable age. Specimens

were examined from 24 cases of cot death, all bottle-fed at the time of death, and early (in respect to the age of the children compared with normal infants) high titres up to 1/512 were found. While these workers did not suggest that the level of serum milk antibody was necessarily a measure of the degree of sensitisation, they claimed that their figures did indicate that the dead infants had received a considerable antigenic stimulation with cow's milk and were hence, potentially at least, sensitised to these proteins. In order to test the hypothesis that aspirated milk protein originated as a regurgitation from the stomach, stomach contents recovered from cases of cot deaths were introduced into the respiratory tract of anaesthetised guinea pigs previously sensitised to cow's milk protein. Only stomach contents from infants known to have been bottle-fed were used. 15 out of 19 guinea pigs died in the manner described, 3 of the survivors showed severe to definite respiratory embarrassment. A control series of 19 unsensitised guinea pigs all survived after the same treatment, one showed moderate, and one mild, respiratory distress. The role of the various protein components of cow's milk in the production of these effects was studied; lethal reactions were produced with whole proteins, casein and beta-lactoglobulin in animals sensitised to whole milk, but only mild reactions followed challenge with alpha-lactoglobulin.

The pathological findings in guinea pigs killed in this way were compared with those found in human cot deaths. In animals dying after challenge with casein or beta-lactoglobulin, the lungs showed general congestion with occasional areas of partial collapse. Serous exudates or oedematous transudates were noted, and there was a cellular infiltrate, mainly mononuclear with many macrophages, a varying number of lymphocytes, sometimes plasma cells and a few polymorphs in the oedematous area or in the peribronchial tissue. The bronchiolar epithelium showed desquamation

of single intact, apparently normal, cells into the lumen. The pulmonary histology of animals dying after challenge with stomach contents from cases of cot death showed a very similar appearance, the cellular infiltration was less marked, but contained more eosinophilic polymorph cells and the desquamation of bronchiolar lining cells was often massive. The appearances described by a number of workers including Barrett(1954) and Stewart (1957) in sudden death in infancy resembled these findings in experimental animals.

This work of Parish and his colleagues (1960a, 1960b) suggests the theory that it is possible that an apparently normal healthy baby could be sensitised to cow's milk when artificially fed; during sleep it could regurgitate stomach contents, some of which might be inhaled and cause an antigen-antibody reaction in the sensitised lung tissue leading to sudden death.

Camps (1963), in a review of unexpected death in infancy, pointed out that much more work would be required before milk sensitisation can be shown to have any significant bearing on this problem. He pointed out that the number of babies who have substantial titres of circulating antibody to milk is large compared with the number of cot deaths and, therefore, if there is any truth in the theory, additional factors may be present, such as a concurrent infection.

Cole (1963) reported the study of 271 cases of "cot" death over a period of 5 years and studied the titres of antibodies to cow's milk in these infants compared with normal babies (in Minneapolis USA). The titres in crib deaths paralleled those found in the controls, which did not support the views of Parish and his colleagues.

Another report from the United States of America (Valdes-Dapena,1963) analysed 113 sudden or unexpected deaths in infancy. This represented slightly more than one half of the total deaths in infancy up to the age

of one year certified in Philadelphia in 1960, an indication of the extent of this problem in modern paediatric practice. 60 of these infants had no evidence of illness at all prior to sudden death, the remaining 53 had a history of minor illness only during a day or two preceding death. Early results of a socio-economic survey showed that the deaths tended to cluster in the slum area. Electrophorectic studies of serum were carried out as Spain et al (1954) had suggested that sudden death in infancy might be due to hypogammaglobinaemia. These studies showed that gammagolobulin levels were not lower in these cases than in a series of control infants of the same ages. Attempts were made to isolate viruses from various organs, techniques included inoculation into adult and suckling mice, chick embryos and tissue cultures of Hela and monkey kidney cells. Only one positive isolate (Coxsackie virus, Group B) was obtained from 109 cases investigated. As far as this worker was concerned, the viral investigations she was able to carry out did not incriminate these agents as being responsible for sudden death in infancy.

Steinberg and Mignery (1963) studied the clinical histories and macroscopic and microscopic findings in 53 infants who died suddenly or unexpectedly. In 21 the cause of death was obvious and from well-defined conditions; the remainder showed what these workers interpreted as acute interstitial pneumonitis of an overwhelming type. The possibility of a viral aetriology was discussed.

Primary acute interstitial pneumonitis as the cause of sudden or unexpected death in infancy was also endorsed by Raven (1963) who reported a disgnosis of this nature in 406 cases out of 475 infant deaths fully examined at autopsy. It was suggested that these infections were the first ones in young, susceptible hosts not previously conditioned by infection (that is, by natural immunisation) and, therefore, more serious. Most of the deaths occurred in the late autumn or early spring months and

paralleled the rise in deaths from respiratory infections in adults.

Socha and Marek (1963) reported that in their experience myocarditis was becoming increasingly common in infants. 22 cases of infant deaths from this cause in the age group 1 - 14 months were seen at autopsy in Cracow, Poland in a period of 3 years, 12 of these had died at home. Death could be sudden, without any prodromal symptoms, or may be preceded by febrile catarrhal infection in the child or its attendants. The autopsy findings were those of acute myocarditis, with hyperaemia, degeneration of muscle fibres and focal or disseminated inflammatory infiltration. In 17 cases these changes were associated with advanced rickets and the authors considered that this was not a coincidence, but that the interstitial myocarditis was due to electrolytic disturbance in the course of rickets.

The epidemiologial aspect was discussed by Sutton and Emery (1966) who reviewed some of the recent literature and hypotheses on the cause of sudden death in infancy. They carried out an epidemiological and microbiological study of 10 such deaths and their contacts, using data re respiratory diseases in families with young children as control material. In a retrospective study of deaths in the period 1961-64 in Sheffield, they found peaks in both the incidence of respiratory disease and of unexpected deaths in infancy on 4 occasions, on each of which an influenza virus was prevalent in the community. In their detailed study of the 10 infant deaths, the incidence of respiratory disease in contacts 10 days before to 10 days after each incident was found to show a peak 2 days before and after the death. Haemolytic streptococci were isolated from 37.9% of the contacts of these infants, but from only 19.6% in a control group. These workers discussed the role of viral infections and pointed out that comparison of various reported studies was unjustifiable as so many factors had to be considered, such as the orientation of the

laboratory undertaking virological studies and the age of the specimen post-mortem. They concluded that the incidence of unexpected death in infancy ran parallel to that of minor respiratory disease in the local community and was especially related to epidemics of influenza.

PART II. CONCLUSIONS AS TO THE CAUSE OF SUDDEN OR UNEXPECTED DEATH IN INFANCY

This part expands the findings in Chapter 3, which were based on the series of infant deaths analysed by me, by reference to the literature on the subject.

In an attempt to decide whether a satisfactory explanation of sudden or unexpected death in infancy has been found, my argument would go as follows:

1. It is an important legal and sociological matter to decide whether sudden death is due to infanticide, accident or natural causes.

It is worthwhile in this connection to reiterate two points mentioned in the review of the literature. Brend (1915), Woolley (1945) and Arey and Sotos (1956) drew attention to the self-recrimination and guilt engendered in the parents when a diagnosis of accidental suffocation is made, and Brend's statement that "it is an extremely cruel thing to leave a mother with the life-long impression that she herself killed the infant unless there is the clearest evidence of the fact" is a most important humanitarian point. On the other hand, one must remember that Barrett (1954) appealed for a clear distinction between practical expediency and scientific accuracy. His view that the attribution of these deaths to fulminant infection on insufficient evidence, for sociological reasons, might mask the true cause and "so delay the cure of an evil which is too apt to be regarded with complacency" must also be given serious consideration.

2. Sudden or unexpected death in infancy can be divided into 2 main groups:

a. Those in which a well-defined cause of death is demonstrated such as is found in death from trauma, major congenital abnormalities, frank meningitis and the like with which diagnosis no one would disagree. This group is in the minority.

b. Those in which autopsy reveals an asphyxial picture, with or without evidence of inhalation of vomitus, or very little apparently abnormal, and in which histological examination shows pulmonary changes, variously described by different authors as slight to severe, and variously interpreted. It is this group, the majority, with which the remainder of this argument deals.

3. There is a general agreement that:

a. These deaths are more frequent during the winter months.

b. They occur mainly in the age group 3 - 6 months.

c. The infants involved do not, as a rule, show any evidence of neglect or faulty care by the parents.

d. Death may occur apparently suddenly, with no prodromal symptoms at all, or there may be a history of minor symptoms which did not give rise to any anxiety.

e. In most cases the infants are found dead in the morning, having been unattended for some hours. Death sometimes occurs during the day, generally the infant had been alone for some time. On occasion, however, infants have been seen to die in the presence of an adult.

These facts are not in dispute, but they must be taken into account in any explanation as to the cause of death.

4. The possibility of infanticide must be borne in mind in all cases of unexpected deaths in infancy. Only a careful history and post-mortem

examination can exclude this. Signs of external pressure on the nose and face, or of trauma to the skull leading to cerebral haemorrhage might raise a suspicion, but it would be very difficult to be dogmatic as to whether death from external mechanical suffocation was accidental or deliberate. Realisation of the entity of the "Battered Baby Syndrome" has become more widespread among the medical and legal professions recently, and in any case at autopsy where an infant shows bruising, a careful examination of the skeleton, including in some cases radiological examination, should be carried out.

A final decision between infanticide and accidental death would depend on skilled appraisal of all the circumstances.

5. Are these deaths due to mechanical suffocation?

a. The earlier interpretation of the cause of death was overlaying and indeed in the circumstances described by Templeman (1892) among the poverty-stricken, ignorant jute-workers in Dundee, this could well have been the explanation in a number of cases. Expert forensic opinion (Smith and Fiddes, 1955) has stated that overlaying is the most common cause of accidental smothering in infancy and that in some cases the parents may be directly to blame if they go to bed under the influence of alcohol and the child sleeps with them. A certain amount of flattening of the nose and cheeks, with pallor of those parts compares with the surrounding lividity, evidence of death from asphyxia, but no evidence of natural disease, are the points brought out by Smith and Fiddes in such cases.

The great majority of infants nowadays, however, occupy separate cots and in most cases described in the recent literature, and in all but two of my series, overlaying can be excluded.

In certain circumstances, therefore, a few cases of death from

overlaying are possible, but this cannot be accepted as the cause of death in the vast majority of cases.

b. Other mechanisms of external mechanical suffocation from bedclothes and soft pillows were for many years accepted as a major cause of sudden death in infancy, but over the past half-century this has largely been abandoned. In the recent literature a single author (Tregillus, 1956) holds that external mechanical suffocation is a frequent event. The reasons for the rejection of this cause of death by most pathologists is based on careful autopsy procedures, including histological examination, pointing to a natural cause of death described by so many authors, the seasonal incidence, the number of cases occurring compared with the vast number of infants at potential risk if this were the explanation and, as a corollary to this, appreciation of the mobility and strength of the normal baby a few months old. A number of cases have also been described (a few in my series) in which sudden or unexpected death has occurred in circumstances, such as in the presence of an adult, in which external mechanical suffocation can be excluded with certainty, but autopsy reveals a picture identical to that seen in infants found dead. It is possible that an ill baby could succumb terminally to external mechanical suffocation, but in this event the underlying illness would be the primary cause of death.

c. Internal mechanical suffocation, by the inhalation of considerable quantities of milk feeds or vomitus, has been postulated as the cause of death. Much the same arguments as in b. above hold here. Quantities of vomitus sufficient to block the main respiratory passages are only found in a minority of cases (in 16 out of 76 in my series), but the history and autopsy findings are the same whether vomitus is present or not in the respiratory tree. The relatively

small number of cases of sudden death, compared with the frequent habit of vomiting in infants, is much against this explanation. Failure of the reflex mechanism protecting the larynx from the entry of foreign material can occur in patients unconscious by drugs or disease (BMJ 1958a), but aspiration of food or vomitus is prevented in normal healthy subjects. In my own experience I have seen massive occlusion of the respiratory tree by vomitus in those dying from severe trauma or alcoholic poisoning and have interpreted this finding as a agonal phenomenon. This is now generally accepted in the case of sudden death in infancy (Camps, 1963).

6. A theory that sudden death in infancy could be due to hypersensitivity cow's milk in artificially fed babies was put forward in 1960 (Parish et al, 1960a and 1960b). Much of their hypothesis was based on experimental work on guinea pigs and interpolation of animal behaviour to man is notoriously dangerous. Apart from a report by Cole (1963) which did not support any difference between the titres of antibodies to cow's milk in infants dying suddenly and those in normal babies, I cannot find any further work on this theory, which by now should have been substantiated or rejected by analysis of the feeding regimes in these infants. My own series did not include this information as the cases were collected before Parish et al published their findings, but I personally have encountered a number of cases since, including Gurkha infants in South East Asia, who were breast-fed. Numerous pathologists have described considerable pulmonary changes in the greater proportion of cases of sudden death in infancy and have considered these to be infective, not hypersensitive, in origin. The incidence versus those at risk and the seasonal incidence are also against this theory.

7. Sudden death, in adults as well as in the young, has been attributed to an enlarged thymus gland. This was mentioned last century (Brouardel

1895) and a diagnosis of status thymaticus (or lymphaticus, or thymolymphaticus) has been accepted by numerous coroners as the cause of sudden death, particularly in anaesthetic fatalities. The normal thymus weighs 13.7 g at birth, increasing in weight until it is 26.2 g at the end of the second year (Ross, 1939). In my series of cases, only one thymus was considered abnormal (weight 32 g), and Farber (1934) stated that no thymus gland was regarded as being pathological in size in a series of 2000 autopsies performed at the Childrens' Hospital, Boston, USA. He considered that the misconception as to a "thymic" state was probably based on erroneous knowledge as to the normal appearance of the thymus gland. A leader in the British Medical Journal (BMJ 1957) considered this diagnosis no longer tenable and it is generally accepted that sudden death in infancy is not due to "status thymolymphaticus" (Camps, 1963).

8. On occasion, myocarditis has been suggested as the cause of sudden death in infants. Henderson (1951) expressed this view and suggested a sequence of mild infection, associated myocarditis and electrical failure leading to cardiac arrest. Such myocarditis, he suggested, may not be demonstrable post-mortem. This would appear to be a negation of the diagnosis.

Socha and Marek (1963) described considerable acute or subacute inflammatory changes in the myocardium in association with severe rickets, but in the remaining series of cases reviewed here there was no suggestion of vitamin D deficiency.

In my series, sections were examined from the heart in 25 instances, no frank case of subacute or acute myocarditis was seen, one case showed myocardial fibrosis of unknown aetiology (case 251) and one, small foci of polymorphs (213). In the very considerable number of cases of sudden death reported in the British, American and Australian literature, myocarditis is rarely mentioned. Bowden (1953) however, diagnosed this as the cause of

death in 8.7% of his 320 cases.

No doubt occasional cases of myocarditis do occur in infancy and can cause sudden death, but the condition would be diagnosed by careful autopsy and would fall into the group of deaths outlined in para 2 a. above, that is a well-defined cause of death, and be excluded from this particular argument.

9. The great majority of pathologists who have been engaged on the problem of sudden or unexpected death in infancy during the past 3 decades now accept the cause as fulminant infection; there are still some dissentient voices. Many series of cases have been published in which careful autopsy procedures have satisfied the worker that pulmonary histological findings are those of various types of pneumonia in the vast majority of cases. In my own series I am satisfied that this is the case.

The seasonal incidence and epidemiological data relating the major incidence of sudden deaths in infancy to that of respiratory disease in the general environment (in particular the work of Sutton and Emery (1966)) is a strong argument in support of this conclusion. One argument against this infective theory is that in some cases the pulmonary changes are but slight (as in 8% of my series). It can be argued, however, that the spectrum of response to acute infections in infancy can include cases in which death occurs from toxaemia before any marked change is detectable in the tissues, this spectrum of response is seen histologically from frank broncho-pneumonia with abscess formation to mild mononuclear interstitial infiltration. As an illustration, one might refer to case 213 (under para 8 of Appendix C).

> An infant aged 4 months was found dead, there were no previous symptoms. The examining pathologist found slight congestion of the lungs and a little greenish mucus in both main bronchi, but nothing else of note, even after histological examination. Review

of the histological material showed slight exudate with scattered mononuclear and polymorph cells in the meninges (figure 135), the myocardium showed hyaline change with occasional polymorph cells between the myofibrils (figure 136), the lungs were congested with areas of acute emphysemia and small areas of consolidation were noted, with thickening of alveolar walls and an infiltration of small round cells, large mononuclear cells, some giant cells and occasional polymorphs in the alveolar walls and spaces (figure 137). The congested spleen showed prominent lymphoid follicles with reactive centres. Though minor in extent, these reactive changes in the meninges, heart, spleen and lungs must suggest an acute infective condition, probably in the nature of an early septicaemia, which killed before producing marked morbid changes.

10. If sudden or unexpected death in infancy is largely due to fulminating infection, what is the aetiological agent? On the whole, the literature on this subject is disappointing as few workers have carried out full microbiological investigations and results differ to some extent. Farber (1934) described the isolation of streptococcus haemolyticus from the heart blood and lungs from cases of this nature. Bowden and French (1951) expressed their disagreement with the belief that after death there was a fairly rapid invasion of the body by micro-organisms from the intestinal tract. This disagreement is borne out by the paucity of positive findings reported in fairly large series (eg, Barrett 1954, Gruenwald and Jacobi 1951 and Banks 1958). Bowden and his co-workers isolated pathogenic or potentially pathogenic bacteria from the lungs in 18 out of 22 cases investigated and in 2 cases recovered an influenza virus. However, Gruenwald and Jacobi (1951) found that special staining techniques failed to reveal organisms in the majority of cases. Barrett (1954) did not consider that the organisms isolated in some cases (staphylococci,

streptococci and haemophilus influenzae) were likely to be important. Arey and Sotos (1956) found 6 bacteriologically proven cases of septicaemia in 10 sudden deaths in apparently healthy children (4 due to pneumococci and 2 to haemolytic streptococci). The steering committee investigating this question in London and Cambridge (Banks 1958), examined 81 cases. The lungs were sterile in 39.4%, normal upper respiratory flora only were isolated in 9.1%, gastro-intestinal organisms with or without normal respiratory tract flora were found in 37.9%, pathogenic organisms, with or without normal respiratory or gastro-intestinal organisms, were only found in 9%. The committee concluded that few of these deaths could be ascribed to bacterial infection as an important factor in sudden death in infancy. Fifty of the 64 cases investigated in London were examined for the presence of viruses, on only 2 cases were positive isolates obtained, in 3 others the presence of a virus could not be excluded. They felt that the crux of their enquiry was intensification of viral investigations. In America, Valdes-Dapena (1963) reported isolation of a virus from only one case out of 109 investigated and concluded that the viral investigations she was able to carry out did not incriminate these agents as being responsible for sudden death in infancy. In my own series of cases I have already concluded that in a proportion some evidence of a bacteriological cause was seen.

Camps (1963), in summarising the position regarding the cause of sudden death in infancy, concluded that "we are left with the equivocal hypothesis of an infection without an infecting agent".

I consider that the extent of knowledge of viruses and virological technique must be given due consideration in this discussion. It is only recently (Morris et al 1956, Chinock et al 1957) that the syncytial respiratory virus was first described. A recent contribution (Anderson 1969) drew attention to the fact that viral infection in children may

produce a reaction quite different to that seen in the adult. In particular, respiratory syncytial virus can produce bronchiolitis which is often fatal. He attributed the severity of viral infection in children to the "narrow physiological margins within which the young infant is able to respire". Dudgeon (1969) drew attention to the extensive involvement of the lower respiratory tract seen in bronchiolitis caused by respiratory syncytial virus in the very young infant. This may be due to a hypersensitivity reaction, possibly due to residual maternal antibody taking part in a local antigen - antibody reaction after infection. This virus has been described as the single most important virological respiratory pathogen in infancy, that is in the first 6 months of life, by Horsfall and Tamm (1965). In the United States of America, Britain and Australia, respiratory syncytial virus is associated with up to 75% of bronchiolitic illness and up to 39% of pneumonic illness of infancy and childhood (Beem et al, 1960). Such illnesses have been described as often life-threatening and in fatal cases interstitial pneumonitis is found (Holzel et al, 1963).

Viruses of the respiratory syncytial and parainfluenzal types are, in common with the majority of viruses affecting the respiratory tract, unstable in character (Swain and Dodds, 1967). Indeed these authors stressed that the only sure way to isolate the respiratory syncytial virus is by direct inoculation into growing tissue culture cells taken to the bedside. It is recorded that 90% of this virus is lost in slow freezing, an important observation in the context of attempted isolation from post-mortem material as cadavers are generally refrigerated before examination and specimens for virological study are generally sent frozen in transit. It would hence appear that the chance of recovering some of the unstable respiratory viruses from autopsy material may be unlikely, though it is of interest that a recent report from the Public Health Laboratory Service

(PHLS, 1969) recorded the isolation of respiratory syncytial virus from a "cot death in a boy aged 4 months (post-mortem trachea swab)" and from a "boy aged 2 months with lower respiratory illness (post-mortem lung)" at two different centres.

The likelihood that respiratory viruses, such as the syncytial type, being the cause of sudden death in infancy bears out the picture often seen in this condition. The failure in the past to isolate a viral agent may well be due to lack of knowledge of these viruses at the time or to the difficulty in isolation by present techniques owing to the unstable nature of many respiratory viruses.

In cases where a bacterial agent has been isolated, it can be postulated that secondary infection has occurred, the bacterial flora of the nose and throat, some potentially pathogenic, invading the broncho-pulmonary system damaged by virus infection (Anderson, 1969).

Professor Camps' conclusion of "infection without an infecting agent" is not such an equivocal hypothesis after all, the infecting agent may be difficult or impossible to recover, but it has done its deadly work.

11. These arguments lead one to conclude that, where an unequivocal cause of death is not found, the great majority of sudden or unexpected deaths in infancy are due to acute infective conditions, septicaemic or pulmonary, bacterial or virological.

12. The final question that requires discussion is whether there is some underlying or predisposing factor in certain infants. Many careful autopsies have been carried out and these infants appear to have no other morbid anatomical defects. Biochemical studies post-mortem, particularly in infants, have received but cursory attention. Spain et al (1954) put forward the hypothesis that sudden death in infancy might be associated with hypogammaglobinaemia, but this has not been substantiated in the series of 114 cases investigated by Vales-Dapena (1963) or by my own

experience. Cruickshank et al (1957) in a small series of cases found that low thiamine serum levels were found in Gurkha infants dying from what they considered to be fulminant pneumonia. As a consequence, thiamine was given to expectant Gurkha mothers, and to their infants when born, in Hong Kong. It did indeed appear at first that the incidence of acute rapidly fatal or sudden death among this infant population did fall, but to my personal knowledge, cases of this nature still occur. This is a biochemical aspect, however, which will repay further study and an investigation into thiamine serum levels in various sections of the population in South-East Asia has been initiated.

It is obviously desirable, in this age when the role of biochemical disorders in medicine is becoming more and more apparent, that further work on chemical pathology in infancy be carried out, but in view of the pathogenesis of respiratory tract infection by viruses in infancy described by Dudgeon (1969), Horsfall and Tamm (1965) and Beem et al (1960) it may well be that these infections can cause death in normal, healthy infants.

CHAPTER 5

DISCUSSION ON INFANT MORTALITY

"But oh! fell death's untimely frost
That nipt my flower sae early"

Robert Burns (1759-1796)

PREAMBLE

The causes of death analysed in Chapters 1 - 3 are consolidated in Table XVIII.

Cause of Death	Neonates	Seriously ill cases	Sudden or unexpected death	Total	
				Number	%
Birth trauma	13			13	5.2
Erythroblastosis foetalis	4			4	1.6
Neonatal asphyxia	21			21	8.4
Respiratory Distress Syndrome	35			35	14.0
Congenital malformations	18	16	4	38	15.2
Infections, all	10	46	58	114	45.6
Respiratory	8	18	56	82	32.8
Central Nervous System	-	5	1	6	2.4
Hepatitis	1	1	-	2	0.8
Peritonitis	-	1	-	1	0.4
Septicaemia	1	3	1	5	2.0
Intestinal	-	18	-	18	7.2
Accidental	1	2	7	10	4
Inconclusive(no histology)	1	-	14	15	6
Totals	103	64	83	250	

Table XVIII - Causes of death in 250 infants

In this chapter it is proposed to discuss the changing pattern of infant mortality over the first six decades of this century and the more important causes of death in this series.

PART 1 - THE PATTERN OF INFANT DEATH

Since the beginning of this century there has been a sustained and dramatic fall in infant mortality; Fig T2 is based on the death rates under the age of one year per 1000 live births in the Registrar-General's Statistical Review of England and Wales, 1960.

Fig T2 - The average infant mortality per 1000 live births per year for each decade from 1841 - 1960

From 1841 until 1900, the average infant mortality over each decade shows very little change, but thereafter the rate has fallen from an average of 153 infant deaths a year per 1000 live births during the period 1891 - 1900, to an average of 25 in the years 1951 - 1960.

The causes of infant mortality of this century have been taken from the 63rd and 83rd Annual Reports of the Registrar-General for England and Wales, 1900 and 1920, and the Registrar-General's Statistical Review of

England and Wales, 1940 and 1960. In 1900 only total numbers were given, in 1920 only rates per thousand, in 1940 and 1960 both numbers and rates are listed. To enable comparison to be made, the figures have been calculated as the percentage number of deaths from each assigned cause. For ease of reference the causes have been grouped into tables:

Table XXIX - Deaths from conditions associated with birth and from congenital abnormalities

Table XX - Deaths from accidental causes

Table XXI - Deaths from acute infectious disease

Table XXII - Deaths from other infective conditions

Table XXIII - Deaths from metabolic and constitutional disease

Table XXIV - Deaths from miscellaneous or unspecified causes

Table XXV - Consolidation of Tables XIX - XXIV

In order to illustrate some points more graphically, skiagrams have been prepared from the data in Table XXV for the years 1900 and 1960, and from the date on all infections for these 2 years; these are shown in Figures T3 and T4.

Cause of death	1900		1920	1940	1960	
	Number	%	%	%	Number	%
Asphyxia(post-natal), Atelectasis	1,225	1.17	1.97	3.8	2,676	15.6
Premature birth (immaturity)	18,476	17.6	23.3	23.6	3,068	17.9
Birth trauma	Not stated		1.52	4.45	1,825	10.65
Congenital malformations	1,516	1.5	5.1	10.9	3,549	20.7
Congenital "debility, atrophy and marasmus"	477	0.46	11.0	3.5	-	-

Total	21,694	20.73	42.89	46.25	11,118	64.85

Table XIX - Deaths from conditions associated with birth and from congenital malformations.

Cause of death	1900		1920	1940	1960	
	Number	%	%	%	Number	%
Suffocation (all Types)	1,924	1.83	0.78	0.82	320	1.87
Other accidents	-	-	-	-	86	0.39
Total	1,924	1.83	0.78	0.82	406	2.26

Table XX - Deaths from accidental causes

Cause of death	1900		1920	1940	1960	
	Number	%	%	%	Number	%
Chickenpox	76	0.073	0.05	-	-	-
Whooping cough	5,508	5.25	2.8	0.98	26	0.15
Measles	3,067	2.9	2.0	0.68	6	0.035
Scarlet fever	170	0.16	0.06	-	-	-
Erysipelas	323	0.31	0.19	-	-	-
Smallpox	3	0.003	-	-	-	-
Diphtheria and croup	432	0.42	0.33	0.016	-	-
Influenza	617	0.59	Not stated	0.98	26	0.15
Total	10,196	9.706	5.43	2.656	58	0.335

Table XXI - Deaths from acute infectious disease

Cause of death	1900		1920	1940	1960	
	Number	%	%	%	Number	%
Tuberculosis, all forms	6,287	6.07	1.74	0.99	10	0.057
Meningeal	1,715	1.63			3	0.017
Abdominal	2,896	2.85			7	0.04
Other	1,676	1.59				
Syphilis	1,154	1.10	1.9	0.27	-	-
Infections of CNS (non-TB)	2,315	2.2	1.07	1.69	187	1.09
Respiratory disease, all	24,318	23.16	21.87	21.07	2861	16.74
Laryngitis	370	0.36	0.15	-	-	-
Bronchitis	13,763	13.1	9.42	4.35	364	2.12
Pneumonia	10,185	9.7	12.3	16.4	2408	14.1
Other	-	-	-	0.32	89	0.52
Intestinal disease, all	19,883	18.97	11.58	7.59	344	2.006
Gastritis	2,244	2.14	1.59	0.29	1	0.006
Gastro-enteritis	17,296	16.5	9.99	7.3	343	2.0
Cholera	343	0.33	-	-	-	-
Other infective and parasitic	369	0.33	-	-	141	0.83
Total	54,316	51.83	38.76	31.82	3543	20.723

Table XXII - Deaths from other infective conditions

Cause of death	1900		1920	1940	1960	
	Number	%	%	%	Number	%
Haemorrhagic conditions	-	-	-	1.39	234	1.43
Haemolytic disease of newborn	-	-	-	0.87	372	2.17
Rickets	508	0.48	0.27	-	-	-
Scurvy	21	0.02	-	-	-	-
Disease of endocrine glands	-	-	-	-	32	0.19

Malignant neoplasms	28	0.027	-	-	55	0.32
Total	557	0.527	0.27	2.26	703	4.11

Table XXIII - Deaths from metabolic and constitutional disease

Cause of death	1900		1920	1940	1960	
	Number	%	%	%	Number	%
Convulsions	16,022	15.3	6.98	2.02	-	-
Lack of care	-	-	-	0.37	32	0.19
Other diseases	1,124	1.07	6.12	13.83	1258	7.36
Total	17,146	16.37	13.10	16.22	1290	7.55

Table XXIV - Deaths from miscellaneous or unspecified causes

Cause of death	1900		1920	1940	1960	
	Number	%	%	%	Number	%
Table XIX - Birth and Malformations	21,694	20.73	42.89	46.25	11,118	64.85
Table XX - Accidental	1,924	1.83	0.78	0.82	406	2.26
Table XXI - Acute Infectious disease	10,196	9.706	5.43	2.656	58	0.335
Table XXII - Other infective conditions	54,316	51.83	38.76	31.82	3,543	20.723
Table XXIII - Metabolic and constitutional	557	0.527	0.27	2.26	703	4.11
Table XXIV - Miscellaneous and unspecified	17,146	16.37	13.10	16.22	1,290	7.55
Total	105,833				17,118	

Table XXV - Consolidation of Tables XIX - XXIV

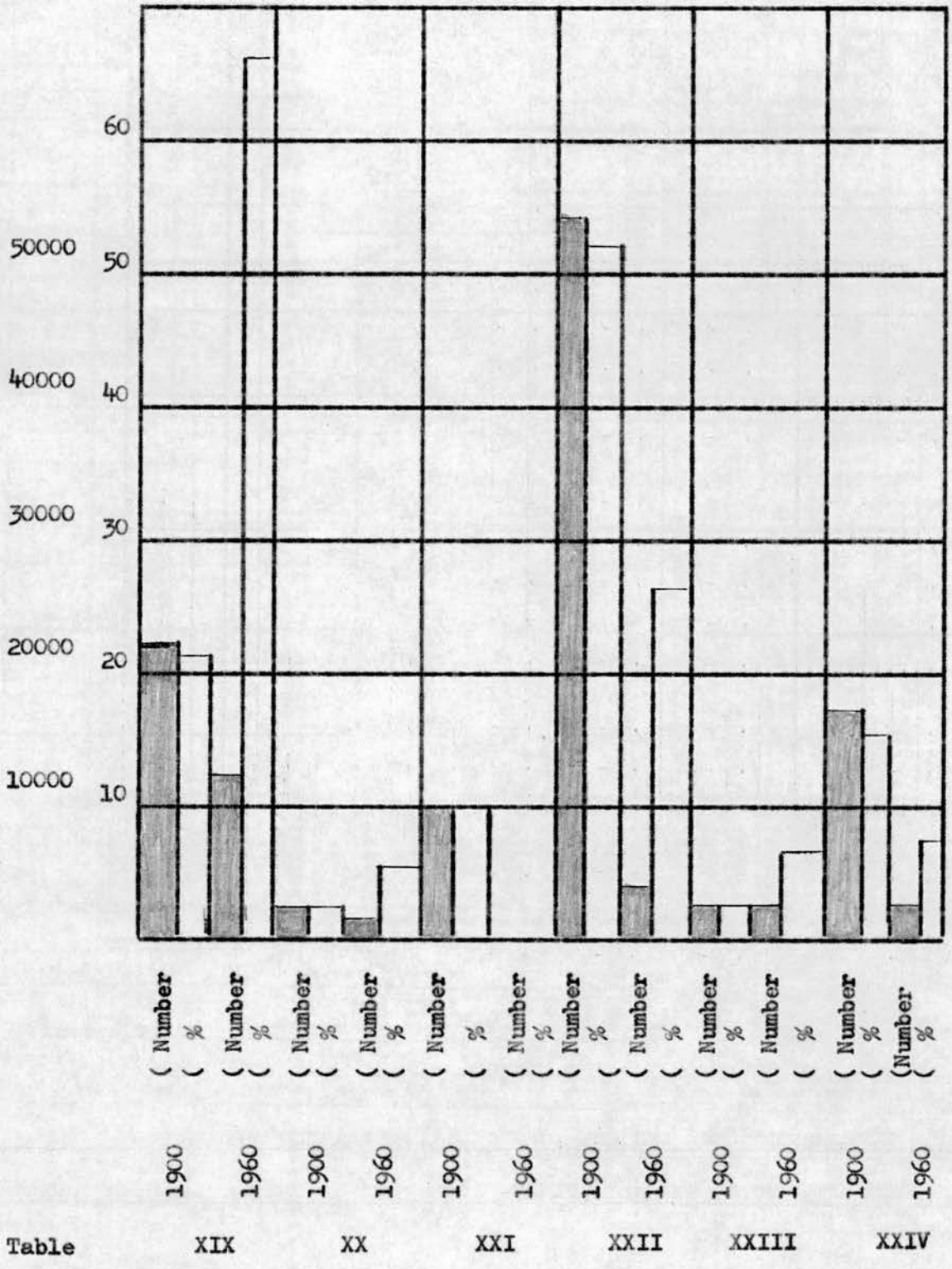

Figure T3. Comparison of the number of deaths, and the percentages, for the six groups of causes shown in Tables XIX - XXIV, for the years 1900 and 1960.

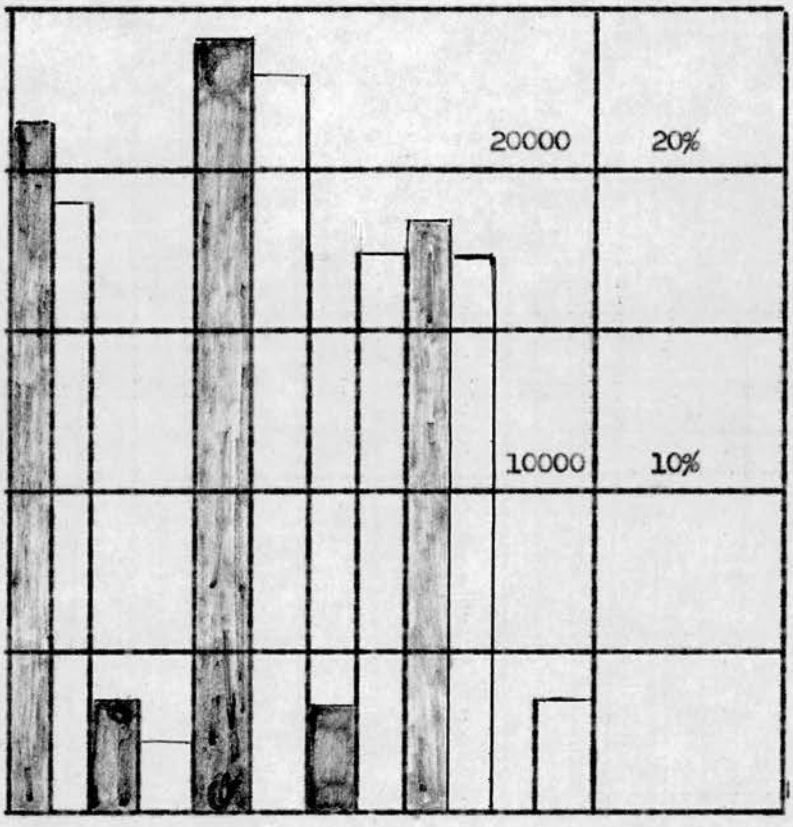

Figure T4. Comparison of the numbers of deaths, and the percentages, from selected infective conditions for the years 1900 and 1960.

Tables XIX - XXIV give a broad, general indication of the trends in infant mortality. Owing to the advances in knowledge and diagnostic accuracy during this century, exact comparisons between some of the causes of death cannot be made; for example in 1900 some 15% of the deaths were ascribed to convulsions, in 1960 this diagnosis was not recorded and there is no means of finding out into which category of definite diagnoses this group should be placed. However, bearing in mind changes in nomenclature and diagnostic advances, a number of interesting conclusions can be drawn.

The infant population in 1900 and 1960 as defined by the number of live births was very comparable, about 700,000 in each of these years. The change in mortality due to infective conditions (Tables XXI and XXII) is the most striking feature of this comparison. In 1900 over 10,000 infants died in the first year of life from acute infectious diseases, the greatest killers being whooping cough and measles, whereas this figure had fallen to 58 in 1960. Other infective conditions fell from a figure of over 50,000 deaths in 1900 to 3543 in 1960. Syphilis has now vanished as a cause of death, tuberculosis is now almost negligible, the incidence of death from infective intestinal conditions is now only about one-fiftieth of what it was at the beginning of this century and respiratory disease, though by no means overcome, now causes about one-tenth the number of deaths. In the sphere of metabolic and constitutional disease (Table XXIII) rickets and scurvy, though not a frequent cause of death in 1900, have now vanished.

In the field of the neonate, however, in contrast to the dramatic fall in deaths from infective conditions, the fall in number of deaths in the group of conditions associated with birth and congenital malformations (Table XIX) has only halved in the six decades under discussion and the number of deaths from asphyxia and congenital malformations has increased some twofold. Some caution is needed, however, in the interpretation of

these figures as the diagnoses are not as clear-cut as in the case of infective conditions.

Of considerable importance is the change in the relative incidence of the various causes of death in this century. In relation to the numbers dying from various assigned causes (Figure T3) there was comparatively little difference in the six groups of conditions, as regards importance, in 1900. Although the total numbers in each group have fallen, dramatically in some, the relative importance of the groups of conditions now shows a marked disparity between numbers and percentages of total deaths. Conditions associated with birth and congenital malformations, from being the cause of death in some 20% of infants in 1900, now account for nearly 65% of the deaths. The proportion of deaths due to all infective conditions has fallen from some 60% to 21%. In this group, however, Figure T4 brings out most convincingly the paramount position of respiratory infections as a cause of death and the virtual absence of the acute infectious diseases.

It may be concluded that this Part focuses the following causes of death to which attention must be particularly paid.

a. Affecting the neonate

Congenital malformations	20.7%	(15.2%)
Premature birth	17.9%	
Asphyxia	15.6%	(22.8%)
Birth trauma	10.6%	(5.2%)
Haemolytic disease of the newborn	2.17%	(1.6%)

b. Affecting all infant age groups

Respiratory disease (particularly pneumonia)	16.74%	(32.8%)
Intestinal disease (gastro-enteritis)	2.006%	(7.2%)
Suffocation (sudden or unexpected death)	1.87%	

The figures in parenthesis are those in my own series (Table XVIII); prematurity per se was not recorded as a cause of death and the majority of sudden or unexpected deaths were ascribed to respiratory disease.

PART 2. THE RESPIRATORY DISTRESS SYNDROME

In the light of present knowledge, the cause of death in neonatal infants showing no specific pathological picture at autopsy, and in whom the clinical picture follows a fairly constant pattern, is recorded as neonatal asphyxia or the respiratory distress syndrome of the newborn.

A considerable number of newly-born infants, particularly those born prematurely, may show difficulty in establishment of respiration accompanied usually by cyanosis, often in attacks, with gradual deterioration, periods of apnoea and death within 5 days, generally on the first day of life. In some cases the condition of the neonate appears initially to be satisfactory, in that respirations are initiated rapidly and the colour is good, but there is then rapid deterioration into the same clinical picture of cyanotic and apnoeic attacks and either death, usually within 12 - 34 hours, or gradual recovery ensues. In fatal cases autopsy, including histological examination, shows a non-specific picture including widespread congestion of organs, often cyanosis of the skin, sometimes petechial haemorrhages in various sites, often complete or partial pulmonary atelectasis, primary or secondary, frequently associated with evidence of inhalation of liquor amnii and incipient or frank hyaline membrane formation in the lungs.

In the past such a condition has been labelled "asphyxia neonatorum" or "hyaline membrane disease", often these diagnoses were qualified by such statements as "due to prematurity". This condition, however, can be found in a wide variety of cases in premature or full-term infants, with or without a history of recognised maternal, foetal or labour complications

or factors. No universal agreement as to the definition of this syndrome has been arrived at as yet, the term "idiopathic respiratory distress syndrome of the newborn" has been accepted by the majority of paediatricians (Rudolf and Smith 1960) although the term "pulmonary syndrome" (Bound et al 1956) is less cumbersome.

The prevention or rewarding treatment of this condition has been stated to be one of the most urgent problems in neonatal practice today. While the incidence of this syndrome as a cause of death has been recorded as some 24% of neonatal deaths (Butler and Bonham 1963, taking their figures of atelectasis with or without hyaline membrane formation), in the present series no less than 55.3% of neonatal deaths are ascribed to it. My definition is somewhat wider than that of other authors as I have included in this category those infants in poor condition immediately after birth in addition to those whose immediate condition appears satisfactory but then deteriorates; the pathological picture in these groups is indistinguishable.

In a considerable number of cases in this series, as in others, incipient or frank hyaline membrane formation is a conspicuous feature in histological preparations from the lungs. This is seen as an eosinophilic hyaline material, in irregular masses, often with squames or other cellular material embedded in it, in the alveoli or lining the alveoli and terminal air passages. While it was long thought that this material was condensed liquor amnii, modern techniques have shown that it is mainly composed of a fibrin-rich protein (enzymatic techniques by Aronson, 1961, or fluorescent antibody studies by Gitlin and Craig 1956). As liquor amnii does not contain fibrinogen and there is little evidence that blood has been inhaled by these infants, it has been concluded that the fibrinogen, and hence the membrane, is derived from transudation of plasma, a form of pulmonary oedema. Such hyaline membrane formation is not confined to the

neonatal condition, but may be seen in older age groups and has been described in pulmonary oedema occurring at high altitudes (Arias-Stella and Kruger 1963), in uraemic pneumonitis (Hopps and Wissler 1955) in influenzal pneumonitis (Soto et al, 1959), in radiation reactions in the lung (Warren and Spencer 1940) and as a result of presumed oxygen intoxication (Buckingham and Sommers 1960). The diagnosis of hyaline membrane disease as a cause of death in infancy is hence no longer tenable.

Recent work is now starting to elucidate the underlying factors in the development of the respiratory distress syndrome. It has been shown that the surface tension of the film of fluid lining the alveoli must be lower than that of other biological fluids (Pattle, 1955), and that it must vary according to the area of the film, that is, the size of the alveolus (Clements et al 1958). The application of the facts led Avery and Mead (1959) to suggest that this low surface tension fluid (called surfactant) was absent in the respiratory distress syndrome. The alveoli therefore collapsed at the end of expiration leading to a low functional capacity. Many of the clinical and pathological features of this syndrome can be explained by this theory which has been supported by the work of Gribetz, Frank and Avery (1956), Clements (1962), and Pattle et al (1962).

Little is as yet known, however, about the mechanisms which can produce a lack of lung surfactant, three explanations have been postulated:

a. There may be a developmental lack of this substance.

b. Surfactant may be destroyed by some other substance (Pattle et al 1962, however, have shown that blood and liquor amnii, at least, do not interfere with this substance).

c. Production of lung surfactant may be dependent on the proper oxygenation of the lung epithelium and hence lack of it may be due to some pre-natal or intra-natal hypoxic episode. Clements (1962) concluded that the final pathway in the production of the respiratory

distress syndrome must be a failure in the surface tension reducing system in the lungs, but it was not yet possible to say if this is the primary defect or if it is secondary to other conditions, that is, whether this syndrome is a sign of functional immaturity or if it is dependent on environmental factors.

As the respiratory distress syndrome is particularly frequent in certain conditions (for example in infants born of diabetic mothers and following maternal bleeding, especially that due to placenta praevia), but is nevertheless found in a wide variety of clinical circumstances, it would appear logical to conclude that the fundamental factor is environmental and the most obvious common factor in this wide variety of situations is hypoxia or anoxia of the infant before or during birth.

The wide variety of clinical circumstances which can produce the picture of the respiratory distress syndrome in neonates can implicate maternal, foetal, or delivery factors, singly or in combination. Some of these factors may result in pre-natal death or intra-interine asphyxia leading to stillbirths, some may result in specific pathological conditions such as frank birth trauma, many result in premature delivery. In a proportion of cases of respiratory distress no such factors may be recognised, but it is not difficult to envisage situations during labour which could lead to dangerous accentuation of the physiological hypoxia of childbirth, but which, apart from careful monitoring of the foetal condition, may not be recognised.

PART 3 - CONGENITAL MALFORMATIONS

About 15% of deaths in infancy in my series were due to gross congenital abnormality, but this is by no means the whole story. Congenital defects can be looked upon as a form of reproductive failure and the whole spectrum of abortions, stillbirths, premature births and neonatal or later death contains an unknown, but probably very considerable,

proportion of cases due to congenital abnormality.

The extent of the problem, as it is reflected in infant mortality, can be gauged by the report that in the United States of America in 1957, 21818 infants died as a result of congenital defect, whereas only one-twentieth of that number (1070) died from the major infectious diseases whooping cough, measles, diphtheria, scarlatina and poliomyelitis combined (Warkany and Fraser, 1964). In England and Wales in 1960, 3549 infants under the age of one year died from congenital malformations, whereas only 58 died from acute infectious disease, including 26 from influenza (Registrar-General, 1960).

If to such infant mortality be added the unknown number of abortions and stillbirths due to congenital abnormality, and the morbidity arising from defects which do not directly kill, but may influence the incidence of premature delivery, with its attendant dangers to the infant, or lead to crippling or breakdown in later life, one can see that congenital malformations have a profound effect on the population from conception to the grave.

But, unfortunately, "little is known about the specific causes of many of the congenital malformations in man" (Nelson 1964a). Intensive epidemiological and genetic studies are under way in many centres throughout the world in an effort to find ways to prevent congenital defects. These studies have already borne fruit and will continue to do so.

Prospective and retrospective studies in man and in animal experiments (the result of the latter cannot with certainty be exterpolated to man) have indicated a number of definite or possible aetiological agents which can be broadly classified as hereditary(genetic) and environmental factors, the latter may be further subdivided into infective, physical and chemical agents. In many cases, however, there is

no clear-cut distinction between hereditary and environmental factors, indeed there is a continuous spectrum from those diseases whose origin is almost completely dependent on genetic make-up (for example, mongolism), through those conditions to which genetic and environmental factors both appear to contribute (for example, schizophrenia) to those diseases which are due solely to environmental experience (for example, cholera).

A. Hereditary (genetic) factors

A genetically determined predisposition to a malformation or disease (Carter 1969a) may depend on a chromosomal abnormality, the effect of a single mutant gene, or the summation of small deviations from normal of numerous genes. Carter has estimated that 1% of all infants born alive have a chromosomal abnormality deleterious to health and that a further 1% will be affected by conditions due to a single mutant gene.

a. Chromosomal abnormalities. The science of medical genetics has grown apace within the past decade and elegant techniques are available for studying the chromosomal make-up of an individual. Many abortuses show chromosomal defects, among children born alive the most common anomalies found are aberrations in the sex chromosomes, for example trisomy, with an extra X chromosome, giving rise to Klinefelter's syndrome in males. Few abnormalities in the autosomal chromosomes have been described, the most important being trisomy of the 21st or 22nd chromosomal pair, causing mongolism (Down's syndrome). While such conditions may be compatible with life for many years, mongol children are particularly susceptible to infection and death generally occurs before the age of 20 years, after a history in most cases of recurrent attacks of pneumonia. This can be the course in the early years of life as illustrated by Case 124 (page 42).

In general, however, chromosomal studies have not implicated major chromosomal abnormalities in the common malformations of the heart and great vessels only; for example, Anders et al (1965) were unable to demonstrate such abnormalities in 156 patients suffering from isolated congenital heart disease.

b. Deleterious genes. While only a few conditions have been shown to be due to demonstrable chromosomal abnormalities, very many (over 1000) conditions have been ascribed to mutant genes ("of large effect", Carter (1969b))although many of these individual conditions are rare.

Abnormalities mediated by mutant genes may be manifest in many ways. Some of these genetic deviations lead to defective metabolism of certain substances or influence the structure or synthesis of some enzymes and haemoglobins. The condition of phenylketonuria, for example, is due to a genetically-determined lack of the enzyme phenylalinine hydroxylase; this lack leads to an accumulation of phenylalanine in the body which may cause serious mental and behavioural disturbances. In galactosaemia, lack of the enzyme galactotransferase means that milk galactose cannot be properly metabolised, the clinical result being serious digestive upset complicated later by cirrhosis of the liver, cataract and mental retardation. Serious neurological complications follow disturbance of the metabolism of leucine in the condition of leucinosis (maple syrup disease).

In certain regions of the world deleterious genes are responsible for defects in red cell production or function, such as is seen in thalassaemia and sickle cell disease.

The familial pattern of diseases due to such mutant genes is determined by whether these are dominant, recessive or sex-linked.

While gene mutations can be increased by agents such as ionising radiations, ultra-violet light and certain chemicals, little is known as yet about such spontaneous mutation in man.

c. Genetic predisposition. There are a number of conditions (for example, inter alia, congenital dislocation of the hip, congenital pyloris stenosis, spina bifida and schizophrenia (Carter 1969c), in which no chromosomal abnormalities have been demonstrated, and in which the patterns are not those of dominant, recessive or sex-linked deleterious genes, but in which there appears to be a genetic predisposition to the disease as shown by family and twin studies. It is believed that additional environmental factors determine whether the disease becomes manifest or not in such predisposed individuals. The recognition of this interplay between genetic and environmental factors is of considerable importance as recognition of, and protection from, the environmental components may prevent the overt disease.

B. Environmental factors

a. Infective agents. A number of microbiological agents can infect the human foetus causing foetal death or post-natal morbidity and mortality. The relationship of some specific agents to congenital malformation is now proven, and as techniques for virus isolation improve, and new methods of antibody detection are introduced, it seems likely that infection will be implicated in an increasing number of such defects (White and Sever 1967). At present a definite relationship has been demonstrated between congenital malformations and three infective agents, the rubella virus, cytomegalovirus and the protozoon Toxoplasma gondii.

(1) Rubella virus was first implicated as a cause of congenital cataract in infants following infection of the mother with

German measles during pregnancy by Gregg (1941). This worker investigated a minor epidemic of congenital cataract in Sydney in the first half of 1941, describing 13 cases he personally attended and reviewing a total of 78 cases from various geographical areas in Australia. It was noted that the affected babies were generally small (average birth weight 5lb), ill nourished, difficult to feed and at least 44 had also congenital cardiac defects. The cataracts, the associated abnormalities of the heart and the widespread geographical incidence suggested a common factor of a toxic or infective nature rather than a purely developmental defect. When the dates of early pregnancy were calculated in the mothers, they were found to correspond with a period in 1940 during which there was a widespread and severe epidemic of rubella. On questioning the mothers, it was found that in all but ten cases there had been clinical infection with German measles, generally in the first or second month of pregnancy. This association between rubella and congenital defects has been confirmed by a number of surveys in different countries. For example, Manson et al (1960) in a survey of 200 British children whose mothers had had rubella in the first trimester of pregnancy, found that the incidence of major congenital defects was 16%, compared with 2.3% in a control group of children whose mothers did not have such a history. This survey also showed that maternal rubella in early pregnancy was also associated with an increased incidence of spontaneous abortion, stillbirth and prematurity. It has now become evident that deafness can also follow congenital rubella infection (Manson et al 1960, Sheridan 1964 and Butler et al 1965).

Proof of virological infection of a foetus was first shown by Selzer (1963), who studied a 20mm foetus delivered by a woman ten days after she contracted rubella. He demonstrated virus invasion of the embryonic tissue and suggested that probably most foetal tissues were so invaded, the involvement varying from massive infection resulting in foetal death and abortion, to lesser grades causing either organic defects in the surviving foetus or no obvious lesions. This work was confirmed by Monif et al (1965) who recovered rubella virus from 3 infants with rubella syndrome defects; in one the virus was recovered before death from the oro-pharynx and at post-mortem examination from no less than ten of eleven tissues studied (lung, liver, brain, kidney, spleen, adrenal, pancreas, thyreoid, thymus and the eye). This work demonstrated the persistence of a chronic state of infection in congenital rubella and the widespread dissemination of the agent.

While the relationship between infection of the foetus with rubella in the early months of intra-uterine life and foetal death, premature delivery and congenital malformation has thus been demonstrated unequivocally, little is as yet known of the way in which the virus attacks foetal tissue (BMJ 1965).

(2) Cytomegalovirus belongs to the same group as herpes simplex virus and in common with it has a tendency to cause latent or symptomless infection (BMJ 1968a). It was first isolated in tissue culture by Rowe et al (1956).

Most viruses cause disease in children more readily than in the adult and congenital infections are often the most severe forms; frequently the mother has a symptomless infection. In the case of cytomegalovirus infection, the effects on the foetus

are more serious if the mother becomes infected in early pregnancy. A general infection of the foetus leads to a syndrome of hepatomegaly, thrombocytopemia and jaundice evident at birth; the virus especially attacks the liver cells so that hepatomegaly is the most constant feature. In later life microcephaly and mental retardation may ensue.

(3) Toxoplasmosis. The causative organism of toxoplasmosis, Toxoplasma gondii, was first described in a small rodent (gondi) in North Africa in 1908, but was not seen in man until Castellani (1914) described finding an organism which appeared to be a toxoplasma in the spleen of a Ceylonese boy who died after a protracted history of fever and splenomegaly. The world-wide incidence of infection with this protozoon was not appreciated until Sabin and Felman (1948) described a serological dye test which is specific (WHO 1969a). While the parasite occurs widely in man, other primates, animals and birds with no apparent host specificity, man himself appears to be highly resistant to clinical disease which is rare compared with the widespread finding of antibodies to toxoplasma in man, for instance in 33% of adults in England (BMJ, 1970a).

The life cycle and mode of transmission of the disease was for many years obscure, but recent work (Hutchinson et al, 1970) appears to indicate that the organism, hitherto generally considered to belong to the subphylum Sporozoa, is in fact a coccidian parasite closely related to the genus Isospora. The route of infection is now established, experimentally at least, as by ingestion.

While symptoms of infection are usually absent or negligible, adults may exhibit lymphadenopathy(Siim's disease, Siim 1956) or

occasionally severe general symptoms with myocarditis and meningo-encephalitis. However, the foetus may be infected from an asymptomatic infection of the mother. The result may be death in utero, or an infected live born baby may develop a variety of systemic and local manifestations with a classical triad of cerebral calcification, chorio-retinitis and hydrocephalus or microcephaly. Systems other than the central nervous system may be affected with combinations of fever, rashes, hepatosplenomegaly, purpura and jaundice (WHO 1969a). The organism may be demonstrated in post-mortem material histologically or by mouse inoculation techniques.

b. Physical agents. The part played by physical agents in the production of foetal abnormalities is still largely obscure. In the shelter of the uterus, the major physical agents likely to be of importance in this respect are hypoxia and ionising radiations.

(1) Hypoxia

In the early months of pregnancy, when maximum organogenesis is taking place, it would appear evident that a reduction of oxygen supply could diminish the rate of growth or bring it to a stop (Potter 1962). If this occurred at the critical period of development of a particular organ, a variety of developmental defects could follow anoxia. Little is known at present, however, of the possible causes of anoxia, and the degree of anoxia which could affect the foetus, in early pregnancy.

(2) Ionising radiations

The most important physical agents known to produce deleterious effects on the developing foetus are ionising radiations. Apart from an increase in neoplastic conditions reported in infants whose mothers underwent radiological

examination while the child was in utero (MacMahon, 1962) congenital defects following irradiation have been reported by a number of workers.

The US Atomic Bomb Casualty Commission has carried out extensive follow-up studies of the survivors, and their children, of the atomic bomb attacks on Nagasaki and Hiroshima. Early assessment gave the impression that low-dose radiation had no adverse effects; later studies, however, on children born to mothers pregnant with them at the time of the bombing, gave the following results:

Dosage range	% of children showing mental retardation
200 rad or more	31%
100-200 rad	9.3%
50-90 rad	4.55%
Nil (women not exposed)	1%

These studies also indicated that children who had been exposed to radiation in the 2nd - 6th month of intrauterine life tended to have smaller heads, and showed a 40% increase in incidence of tumours of the central nervous system, than those unexposed.

The likelihood of pregnant women being exposed to dosages of ionising radiations of these orders, however, is remote in normal circumstances and the part played, if any, by low doses of radiation in the diagnostic range, if unknown.

Fraser (1967) also indicated that therapeutic levels of radiation in early pregnancy can cause microcephaly, and skeletal deformities in the embryo, but that whether somatic damage follows diagnostic levels of radiation is unknown. It is of interest, however, to note that in a study in New York State, Gentry et al (1970) found that the incidence of congenital

malformations of all types, excluding mongolism, was significantly increased in an area which had an unusually high background of natural radiation.

Carter (1969d) stated that ionising radiations, which were only increased for practical purposes in man by diagnostic radiology, could increase gene mutation.

c. Chemical Agents. A considerable literature has been built up on the subject of the influence of chemical agents in the production of foetal malformations. The role of some has been substantiated, some have been implicated but not proven, some have produced a diversity of opinion and some appear to be innocuous in this context.

The tragic "epidemics" of phocomelia and amelia described mainly in Germany, Great Britain, Italy and Sweden as the result of the use of the tranquiliser thalidomide in pregnancy (Rubin and Freidenberg, 1967) is still fresh in one's mind.

Fraser (1967) reviewed the position concerning a considerable number of drugs in relation to foetal malformation. Alkalating agents have been shown to be highly teratogenic in rats and there is strong presumptive evidence that drugs such as chlorambucil, cyclophosphamide, busulfain and 6-mercaptopurine can produce these effects in the human. This author stated that there are grounds for caution in the use of chloroquin in pregnancy and that antimetabolites, such as aminopterin, and carbon monoxide poisoning have been implicated in foetal defects. There was no valid evidence that antibiotics, malnutrition or progestational agents caused malformations.

As knowledge increases, however, such reviews may require amendment. As regards salicylates, Fraser stated that these drugs are "almost certainly not teratogenic in usual doses". Very large

doses of salicylates given to pregnant rats produced malformation in the young (Warkany and Takacs, 1959) and even aspirin could have the same effect in rats and mice (Trasler, 1965; Takacs and Warkany,1968), but again the dose required to produce these effects was considerably greater than anologous therapeutic doses in man. A retrospective study of 833 pregnant women who had given birth to malformed children, and an equal number of controls (women of similar age, parity, social class, area of residence and date of delivery, whose pregnancies resulted in healthy babies without malformations), was reported by Richards (1969). A history of taking salicylates in the first four months of pregnancy was given by 22% of the mothers with deformed children, but by only 14% of the control group. Little difference (28% and 24% respectively) was found in these 2 groups when the drug had been taken after the 16th week of pregnancy. In commenting on these findings the BMJ(1970b) stressed the need for care in the interpretation of retrospective studies of this nature, and considered that the question as to whether salicylates in therapeutic doses in pregnancy could cause foetal malformations was still unanswered. Further work was in progress on a larger survey.

In his review, Fraser referred to the possibility of cortisone being implicated in the production of cleft palate defects. While the work reviewed below suggests an inimical effect on the human foetus of drugs of this nature, not necessarily the development of specific malformation, it is included here to stress the controversial nature of the effect of drugs in pregnancy. Deleterious effects of cortisone on mouse pregnancies were reported by Fainstal and Fraser (1951), but Yackel et al (1966) and Walsh and Clarke (1967) in reporting their analysis of a series of cases showed that the risk to the human foetus was small. In contrast, however, Warrell and Taylor

(1968) reported otherwise. An analysis of the outcome of 34 pregnancies in women receiving prednisolone for a general disease (mainly eczema and asthma) showed that 8 infants of these pregnancies were stillborn, 9 infants were in a poor state at birth and required skilled care and one infant unexpectedly developed a severe respiratory distress syndrome. Thus in 18 cases out of 34, more than 50%, the foetus was either stillborn or at considerable risk. In a control group, women matched for the same disease of similar severity, of the same parity and approximately the same age, but not receiving steroid therapy, the pregnancies resulted in 30 healthy babies, one stillborn and 3 premature babies, a mortality and morbidity figure of some 12%. These workers suggested that the effect of the drug was on the placenta, rather than on the foetus, causing placental deficiency in analogy with experimental work on rats reported by Blackburn et al (1965) in which the administration of prednisolone caused premature ageing of the placenta and an increase in intrauterine deaths.

One may conclude this section by reiterating that, though some chemical agents given to pregnant women have shown to produce foetal malformations, the role of many others is still controversial and much further work must be done before any particular drug can be declared completely innocuous in this respect.

PART 4 - ERYTHROBLASTOSIS FOETALIS

Although the cause of erythroblastosis foetalis was not established until the discovery of the Rh blood groups by Landsteiner and Wiener(1940), echoes from the past pointed toward the aetiology and pathology. In 1923, Ottenburg, who was working on the cause of eclampsia, suggested that "accidental placental transfusion" of incompatible blood might cause jaundice in the newborn. Cruikshank (1930), in discussing the causes of

neonatal death, described a case of splenomegaly in his series. A mother who had had a child that died on the ninth day after birth, then a miscarriage, gave birth to a third child which became jaundiced the following day and by the third day of life was seriously ill; feeble, cyanosed and jaundiced with gross enlargement of the liver and spleen. It died on the fifth day; histological examination showed underspread infiltration of the liver and spleen with embryonic blood cells, not so definitely in groups, Cruikshank wrote, as seen in congenital syphilis. While he concluded that this was possibly a case of congenital leukaemia, the clinical description and pathology are strongly suggestive of erythroblastosis.

Levine and Stetson (1939) reported that a mother, who had just been delivered of a stillborn infant, developed a severe reaction when transfused with her husband's blood, although both were Group O. Further cross matching showed that the woman's serum did agglutinate with her husband's red cells and also with red cells from 80 out of 104 group O donors. The interpretation put upon this was that the mother had become immunised by her foetus which possessed an antigen which she lacked, and which had been inherited from the father. The maternal antibody had reacted with this antigen in her husband's red cells and caused the transfusion reaction.

Landsteiner and Wiener (1940) prepared an antiserum from rabbits and guinea pigs inoculated with blood from a rhesus monkey (Macacus rhesus) and discovered that this serum agglutinated the red cells of about 85% of white people in New York. They termed these reactors "Rh positive" and the remaining 15% "Rh negative". The antibody described by Levine and Stetson above was found to be the same as this rabbit anti-rhesus antibody. Thus the Rh group was discovered and further British and American work elucidated the whole system (Race and Sanger, 1950).

The relationship between Rh incompatibility and erythroblastosis was demonstrated by Levine and his co-workers the year following the discovery of the Rh groups (Levine et al, 1940a, 1940b). This extract from the latter reference sums up the basic aetiology of the condition. "Erythroblastosis foetalis results from (1) iso-immunisation of the mother by dominant blood heredity factors in the foetus, as evidenced by the production of immune intra-group agglutinins, and (2) the subsequent passage of these maternal agglutinins through the placenta and their continued action on the susceptible foetal blood".

While a number of Rh antigens, and those from other blood groups such as the Kell system, may cause haemolytic disease of the newborn, the great majority are due to maternal sensitisation with the Rh D antigen(Mollison, 1964).

The continuous action of antibody on the foetal blood, with resultant haemolysis, is the basic pathological change, almost all the clinical and pathological features being directly dependent on this. Haemolytic anaemia leads to anoxaemia and an increase of free bilirubin. Anaemia and anoxaemia cause increased permeability of the capillary walls, with resultant oedema, cardiac enlargement and haemic murmurs. The increase in bilirubin leads to jaundice and sometimes kernicterus. The anaemia also leads to a compensatory erythropoetic activity which results in widespread extra-medullary foci with hepato-splenomegaly and the presence of numerous nucleated red cells in the peripheral blood. The increase in lipid deposition in the adrenals and the hyperplasia of the Islets of Langerhans in the pancreas may be due to disordered metabolism consequent on the anaemia. In addition to the laboratory findings expected from this fundamental pathology (a profound fall in the red cell count, initially many cells being nucleated, and high serum bilirubin levels), the cells of the infant, being sensitised by maternal antibody, give an agglutination reaction with an anti-human globulin serum(a positive direct Coombs' Test).

The susceptibility of women to sensitisation by a foreign blood antigen in a foetus varies considerably, and an Rh negative X Rh positive mating, resulting in an Rh positive foetus, does not necessarily lead to sensitisation. In first pregnancies initial sensitisation, if it occurs, is too late and too weak to affect the foetus so that erythroblastosis by this mechanism (primary foetal sensitisation), if it occurs at all, generally appears in the second or subsequent pregnancies. Sensitisation by blood transfusion, however, is more likely to stimulate antibody formation and probably explains cases of erythroblastosis occurring in first pregnancies (Nelson, 1964b). In assessing the incidence and dangers of sensitisation, it must be borne in mind that most Rh positive men are heterozygous as regards the D antigen so that only about half of their offspring will be antigenic in this respect to an Rh negative mother.

Although some 12% of marriages are of Rh negative women to Rh positive men, the heterozygous factor in the father, and the varying susceptibility of women to sensitisation, results in the incidence of erythroblastosis being only about once in every 200-250 pregnancies and at the present time this condition accounts for 2-3% of all neonatal deaths. The severity of the disease varies, the severe jaundiced form occurring about once in every 1500 pregnancies and the fatal hydrops type about once in every 2000 pregnancies (Boyd, 1958).

PART 5 - INFECTIONS IN INFANCY

A - RESPIRATORY TRACT INFECTIONS

The changing pattern of the causes of infant mortality discussed in Part 1 of this Chapter highlights the increasingly important part played by respiratory infections, particularly in the post-neonatal period. The comparatively high mortality in the first 2 weeks or so after birth, due to the complications of prematurity, birth trauma and malformations of a severe nature, rapidly declines in the post-neonatal period and in the

next year of life infections (including the majority of cases of sudden or unexpected death in infancy) and, to a lesser extent, metabolic diseases and accidents, dominate the picture. The final columns of Table XXV highlights this.

Cause of death		% of deaths in 1960	
Associated with birth and malformations		64.85	
Accidental		2.26	
Acute infectious disease		0.335	
Other infective conditions All		20.723	
	Respiratory	16.74	)Table
	Intestinal	2.006	) XXII
Metabolic and constitutional		4.11	
Miscellaneous and unspecified		7.55	

More than half of the deaths in the first year of post-neonatal life after the immediate post-natal period are due to infections of the respiratory tract.

The pattern of respiratory disease in infancy itself appears to have changed during this century, partly due to an increase in knowledge, particularly in the field of virology. In the Section of Diseases of Children at the Annual Meeting of the British Medical Association in Edinburgh, 1927, McNeil and Macgregor reviewed 558 cases of acute pneumonia treated in the Edinburgh Hospital for Sick Children in the years 1920 - 1927. Their figure for age incidence and mortality rates are reproduced in Table XXVI.

Age Incidence	Cases	% Mortality
Birth - 1 year	119	42.8
1 - 2 years	160	20.6
Birth - 2 years	279	30.1
3 - 12 years	279	5.7

Table XXVI - Age incidence and percentage mortality in 558 cases of acute pneumonia. (After McNeil and Macgregor, 1927)

It is clear that at that time, as today, respiratory infection was more common, and much more deadly, in the first 2 years of life than in later childhood.

Macgregor discussed the pathological findings at autopsy in these cases, describing 2 varieties of pneumonia, lobar and broncho-pneumonia. In 100 autopsies lobar pneumonia, characterised by alveolar exudate, with a remarkable absence of inflammatory infiltration of the interstitial framework, including the lymphatic system, was found in 11 instances. Great variation was found in the extent of the consolidation and it was suggested that, in the child, "alveolar" would better describe the pneumonia than "lobar". Three of these 11 cases were bilateral. The remaining 89 cases showed broncho-pneumonic changes, bilateral in 79, characterised by a substantial inflammatory infiltration of the substance of the bronchi and alveolar walls including the lymphatic system. Alveolar exudate and consolidation appeared to be preceded by this acute interstitial inflammation which was judged the essential part of the pathological process. This led the author to suggest the term "interstitial" rather than "broncho" pneumonia, a term widely used by later authors.

In the discussion on aetiology, it was pointed out that broncho-pneumonia is known to follow measles and influenza and that B influenzae had been isolated in a number of cases (McNeil). Macgregor also suggested that there may be a primary aetiological agent in the form of a virus of special quality, an astute prognostication of the isolation of viruses such as the respiratory syncytial virus some three decades later. Speakers from the floor suggested that all primary pneumonias in childhood were due to the pneumococcoccus (Thursfield) or that many (21 out of 33 autopsies) yielded an isolate of influenza bacilli (Glen Liston).

Macgregor (1947) further commented on neonatal pneumonia twenty years later. In the first few days of life pneumonia generally affected lungs in which the alveoli were abnormal as a result of birth stress, such as atelectasis resulting from respiratory depression due to severe asphyxia, or a water-logged state due to excessive aspiration of liquor amnii often seen in anoxic states. Septic pneumonia followed the inhalation of milk or regurgitated stomach contents resulting in severe, destructive inflammatory changes in and around the bronchi, often followed by suppuration. She considered that staphyeococcal pneumonia, leading to rapid abscess formation, was found more commonly in the young infant than at any other period of life. Broncho-pneumonia at this age followed a pattern similar to that seen in older children, the causal organisms being those of the respiratory tract, with the addition on occasion of coliform organisms, not generally found in older subjects.

Potter (1962) divided the pneumonias of infancy primarily into two groups. In the first few days of life, infection was usually of intra-uterine origin from contamination of the foetal environment, particularly common when there was a protracted second stage in labour and difficult delivery. The attendant anoxia with increased respiratory activity contributed to the establishment of infection. In these cases both the clinical diagnosis and the interpretation of the gross appearance of the lungs at autopsy were difficult, and diagnosis depended on histological examination.

In the post-natal period a number of types of pneumonia were described. While pneumococcal infections were rare, broncho-pneumonia might become confluent and give a gross appearance of lobar pneumonia. Destruction of tissue appeared to occur more readily in these young infants than in older age groups and abscess formation was common. The severity of the pathological lesions, however, did not, in many instances, bear much

relation to the outcome. Some infants dying after pulmonary symptoms showed remarkably little evidence of pneumonia at autopsy, merely an inflammatory oedema or an interstitial type of infection. On the other hand, infants with no signs of pulmonary involvement might show definite pneumonia at autopsy.

A leading article in the British Medical Journal (BMJ 1958b) discussed an acute respiratory disease of babies with a high incidence in London and Birmingham. The diagnosis of bronchiolitis was accepted as a distinct entity, a serious, alarming condition with a high mortality. Because of diagnostic difficulties, the incidence of this condition was difficult to determine, but the clinical syndrome appeared well-defined. The infant had an initial mild coryzal illness (often other members of the family had 'colds') or gastro-intestinal symptoms. Deterioration followed with dramatic rapidity a few days later with the development of severe pulmonary symptoms, hypoxia, cardio-vascular collapse and a moribund state developed within a few hours in severe cases. Histologically, the predominant finding in the lungs was blockage of the bronchi and bronchioles with mucus plugs or a mucopurulent secretion and inflammatory swelling of the bronchial epithelium. Congestion was evident and the cellular component of the exudate was mononuclear rather than purulent. The aetiology of the condition was uncertain.

Considerable advances in the understanding of this condition have been made during the past decade. The expanding field of virology, particularly the discovery of the respiratory syncytial virus (RSV) Morris et al 1956; Chanock et al, 1957a, 1957b) has led a number of workers to the conclusion that bronchiolitis in infancy is generally of viral origin, initially at least. Horsfall and Tamm (1965) described the RSV as the single most important virological respiratory pathogen in the first six months of life. In fatal cases they described an interstitial pneumonia which may have a

purulent component added by a secondary infection with pathogenic bacteria. In the United States of America, Great Britain and Australia, the RSV is associated with 32-75% of bronchiolitic illness and in up to 39% of pneumonic illness in infancy and childhood (Beem et al, 1960). Such illness is often life-threatening (Holzel et al, 1963).

The difficulties in determining the aetiological agent in many cases of this nature have been discussed by Swain and Dodds (1967). The majority of the viruses affecting the respiratory tract fall into the category of the unstable viruses which do not survive more than a few hours outside the body under ordinary atmospheric pressure. The only sure method of isolating the RSV is by direct inoculum into growing tissue cultures taken to the bedside. At present the inevitable delay in virological diagnosis means that such diagnosis is largely retrospective and hence academic. The development of direct fluorescent techniques, however, may enable rapid virological diagnosis to be made and consequently, a better understanding of the role of these agents in disease of the respiratory tract. These authors stressed that the severity of infections of this nature with RSV and other viruses in infancy was due to the narrow physiological margins within which a young child is able to respire.

Dudgeon (1969) suggested that the extensive involvement of the lower respiratory tract in cases of bronchiolitis caused by RSV in the very young may be due to a hypersensitivity reaction between the virus and residual maternal antibodies.

Anderson (1969) considered that most respiratory infections in infancy were associated with viral or other non-bacterial infections.

Analysis of the cases of pneumonia in neonates, in infants dying after serious illness and in infants dying suddenly or unexpectedly in my series has been carried out.

The macroscopic findings are shown in Table XXVII.

	Total Cases	Upper Respiratory Tract Infection	Pneumonic Consolidation	Abscess Formation	Pleural involvement
Neonates	8	1	8	2	3
Those seriously ill before death	18	10	18(a)	3	11
Sudden or unexpected death	70	23	27	1	7

Table XXVII - Macroscopic findings in 96 cases of pneumonia in infancy

Note: In only a proportion of cases of sudden or unexpected death was there naked eye evidence of pneumonia.

Note: (a) One typical lobar distribution.

Histological examination was carried out in 4 of the neonatal cases and in 11 of those dying after a period of serious illness; the predominant type of cellular response is shown in Table XXVIII.

Type of cellular infiltration	Neonates	Seriously ill group
Polymorphonuclear	2	7
Mononuclear	1	2
Mononuclear with giant cells	1	2
Plasma cells		1

Table XXVIII - Microscopic findings in 16 cases of pneumonia in neonates and those infants seriously ill before death

In the group of infants dying suddenly or unexpectedly, analysis of the pulmonary histology in 52 cases showed that upper respiratory tract infection was present in 34 and pneumonic changes to some degree in all. The types and site of cellular infiltration in these cases are shown in Table XXIX.

	Type of cellular infiltration			
	Polymorphonuclear	Small Mononuclear	Large Mononuclear	Giant Cells
Interstitial	39	30	38	3
Alveolear	11	13	39	13

Table XXIX - Type and site of cellular infiltration of the lungs in 52 cases of sudden or unexpected death in infancy

Many cases showed a picture varying in areas from an acute polymorphonuclear type of pneumonia to an interstitial mononuclear type in different fields of the same section and there is hence overlapping in the above table.

In general, however, one type of picture predominated and it was felt possible to classify the type of pneumonia broadly into the following groups on histological grounds.

1. Cases in which the picture was that of a classical broncho-pneumonia with an inflammatory infiltrate, predominantly polymorphonuclear, surrounding the smaller bronchi and bronchioles which were often disrupted, with an exudate and similar infiltrate in the surrounding alveolar tissue causing patchy consolidation.

2. Cases of a similar nature as regards distribution, but where the inflammatory infiltrate was of small or large round cells, giving a mononuclear type of broncho-pneumonia.

3. Cases in which the inflammatory infiltrate was largely confined to the lung interstitium, the walls of alveoli being thickened, but the alveoli being relatively free. These cases could be further sub-divided into those:

   a. where the infiltrate was predominantly polymorphonuclear,

   b. where large and small round cells predominated and

   c. a single case where the infiltrate was predominantly of plasma cells (accompanied by the presence of pneumocystis carinii in the alveoli).

4. Cases of mononuclear pneumonia of the categories 2 and 3b above where a number of giant cells were present.

The distribution of these histological types of pneumonia are shown in Table XXX:

		Neonates	Seriously ill cases	Sudden or unexpected death
Broncho pneumonia	Polymorphonuclear	2	7	17
	Mononuclear			4(17)
Interstitial pneumonia				
	Polymorphonuclear			14
	Mononuclear	1(2)	2(4)	1(4)
	Plasma cell			
Giant cell pneumonia		1	2	16

Table XXX - Microscopic classification of cases of pneumonia

(Note: Figures in parentheses show the total number of cases of mononuclear pneumonia, 19 of which also showed the presence of giant cells).

From Tables XXVII - XXX the following conclusions may be drawn.

In the neonatal group, taking into account both macroscopic and microscopic findings, a classical type of polymorphonuclear broncho-pneumonia was the usual picture, with abscess formation in two and pleural involvement in three.

Similarly in the group dying after serious illness, a classical broncho-pneumonia was seen in 12 cases, lobar pneumonia in one, mononuclear in 4, two of which also showed giant cells and a plasma cell pneumonia in one. Macroscopic abscess formation was seen in 3 cases and pleural involvement in 11, two of which showed empyema.

The findings in the group who died suddenly or unexpectedly are based on microscopic findings. In 31 cases the polymorphonuclear component predominated, in 21 the picture was that of a mononuclear type, in 16 of which giant cells were also present.

In only a minority of all cases of pneumonia in this series were potentially pathogenic bacteria(mainly strains of staphylococci) isolated, and no correlation has been found between these types of pneumonia and the recovery of an organism. The very few virological studies made were negative.

The interpretation of these findings, mainly based on microscopic appearances, taken in conjunction with the clinical picture and the views expressed by authors quoted above suggests that we are dealing with a spectrum of pathological change rather than with a series of well-defined and separate pathological entities (exceptions are the cases of lobar pneumonia and pneumocystis pneumonia which will be excluded from this argument).

It would appear that the spectrum of pneumonia in infancy has 3 main facets:

1. An acute bacterial aetiology ab initio, characterised by a predominantly polymorphonuclear type of infiltration leading to the classical type of broncho-pneumonia, often complicated by abscess formation or pleural involvement. This type is frequently seen in the neonate and (Potter, 1962) is dependent on adverse factors in the foetal environment during labour. Some cases occurred in those seriously ill before death, often being complications of other causes of morbidity such as previous prematurity, other bacterial infections and congenital abnormalities.

2. A viral pneumonitis, characterised by frequent upper respiratory tract involvement and a mononuclear type of cellular infiltration, often associated with the presence of giant cells, and particularly affecting the interstitial tissue of the lungs. In addition to the authors already cited in this Part, one may note that Boiset y Boiset (1946), in an analysis of 875 fatal cases of pneumonia in childhood, found that 15% fell into the category of interstitial pneumonia characterised by an infiltration of mononuclear cells into the walls of alveroli, interlobular septae and the peribronchial and perivascular tissue. These cases followed measles or whooping cough. Wolman et al (1952) described 5 cases of interstitial giant cell

pneumonia and concluded that this diagnosis and viral pneumonia in infants represented a single disease entity. The Lancet (1960) concluded that measles virus was the cause of some cases, at least, of giant cell pneumonia.

The lability of the majority of viruses affecting the respiratory tract explains the paucity of positive isolations from post-mortem material in these cases.

3. A mixed picture, characterised by areas of polymorphonuclear infiltration interspersed by areas of mononuclear inflammation (with or without giant cells). This type was seen particularly in those dying after a period of serious respiratory illness and in a proportion of those dying suddenly or unexpectedly.

This picture is interpreted as being the result of a secondary bacterial invasion of an acute bronchiolitis or pneumonitis of viral origin; a primary measles infection was found in a few cases in my series, but in general no viral agent has been isolated, although a number of authors incriminate the respiratory syncytial virus.

It may therefore be concluded that, althogh histological types of pneumonia such as acute broncho-pneumonia, interstitial pneumonia, mononuclear pneumonia and giant cell pneumonia have been described by many authors, the clinical and total morbid-anatomical picture is that of a spectrum of disease of primary viral or bacterial origin with many cases showing a combination of the effects of these two main classes of infective agent. In life specific diagnosis is generally very difficult.

B - GASTRO ENTERITIS

Gastro-enteritis was the cause of death in 7.2% of the infant deaths analysed by me. An analysis of the causes of death in 679 babies aged one month to one year (a more restricted age group) showed that 14% died from diseases of the digestive system (DHSS, 1970).

The true incidence of gastro-enteritis in this country is not known, as the disease is not notifiable, but it is estimated (Ironside et al, 1970) that 10,000 infants are admitted to hospital yearly from this cause and that only about 10% of cases arising in general practice are referred to hospital. These figures suggest an incidence in Great Britain of some 100,000 cases per year which resulted in 400 deaths in 1967 in children under the age of two years (Registrar's Office, 1969). As a cause of very considerable morbidity and a not inconsiderable mortality, gastro-enteritis is an important disease in paediatric practice.

Aetiology. There has been a change in the pattern of infantile gastro-enteritis during this century. In the earlier years summer diarrhoea, often occurring in epidemics, and most frequent in the second year of life, was of major importance (Wilson and Miles, 1964). This disease, however, has now practically disappeared from Great Britain, probably associated with improvements in hygiene. Nowadays, gastro-enteritis in infants shows no seasonal incidence, the disease is sporadic in the general infant population, although outbreaks are reported among neonates in maternity hospitals and infants in institutions.

Many bacterial causes have been incriminated, but in many cases no casual agent is isolated. Granblatt and Siewers (1965) carried out extensive studies on a world wide basis and reported that pathogenic bacteria were isolated in 22-64% of cases. Species of Shigella and Salmonella are common causes of infantile diarrhoea in tropical and sub-tropical countries, but are not frequently isolated in this country (Taylor, 1951).

Since the observations of Bray (1945) that a particular strain of Eschereria coli was associated with an outbreak of severe gastro-enteritis in infants in hospital, it has become apparent that a number of strains of this organism are enteropathogenic; of the 150 or more serotypes which

have been described, at least 10 are particularly associated with infantile diarrhoea.

The role of virus infections is still debatable. On occasion enteroviruses, particularly strains of the ECHO virus and adenoviruses, have been incriminated, but conclusive proof of their pathogenicity in this respect is lacking (BMJ 1969a).

Morbid anatomy. MacGregor (1960) commented on the paucity of pathological changes in fatal cases of infantile gastro-enteritis. The bowel is thin-walled and often pale, congestion if present is generally confined to the upper part of the small intestine, macroscopic and microscopic evidence of inflammation is frequently absent, erosion and ulveration is rare.

The cases analysed by me showed a gross picture of dehydration, but the local changes in the intestinal tract were not marked. Congestion, thinness of the intestinal wall, with some inflammatory cell infiltration of the bowel and regional lymph nodes were the main, but rarely marked, features.

Biochemical changes. Ironside et al (1970) showed that the commonest electrolytic abnormality, consequent on dehydration and becoming more marked as dehydration became more severe, was hypernatraemia (levels of plasma soldium over 150 m Eq per litre being found in 63% of all cases of gastro-enteritis). Standard bicarbonate levels showed a metabolic acidosis in 56%, but no correlation was found between the degree of acidosis and the state of dehydration. Blood urea levels were above the upper limits of normal (40 mg per 100 ml) in 88%, the highest figures being found in patients most severely dehydrated, the mean figure in this group being 152 mg per 100 ml.

Clinical features and course. In most of the cases recorded by me the history was that of diarrhoea and vomiting with, in general, the

development of dehydration which did not respond to parenteral fluid therapy and antibodies, or in some cases showed initial response to these measures with subsequent relapse. The duration of the illness was generally short, from one day's severe, almost choleriac, diarrhoea and vomiting to five day's symptoms of increasing severity. Four cases out of 18 had a chronic course lasting 2 - 4 weeks with gradual deterioration and death in a marasmic state. Six of the cases showed involvement of the respiratory system or other infective process. The majority occurred in the age groups six months or less, no seasonal trend was noted.

This analysis was from the clinical histories of infants dying from the disease. In their survey of gastro-enteritis Ironside et al (1970) based their findings on 339 hospital admissions for infantile gastro-enteritis, five were fatal. The clinical picture described by them is therefore a more general one. Diarrhoea and vomiting was accompanied by dehydration in 33%, most of the latter also showed fever and tachycardia, correlated in degree with the severity of dehydration. Haemoglobin values below 9.6g per 100 ml were found in 25% of these admissions, but there was no significant correlation between anaemia and the degree of dehydration.

The younger age group (less than 3 months) formed the largest and more cases occurred in the Oct - Dec period. There was an associated upper respiratory infection in 64% and urinary infection in 1%.

This survey from a regional infectious diseases unit serving a large urban industrial area appears to mirror the problem of infantile gastro-enteritis in this country at the present time - a mainly sporadic disease, but occurring sometimes in small epidemics in neonatal units and infant institutions, from which in general no casual agent can be found, though in a proportion enteropathic strains of E coli are isolated. Pathological changes are not marked locally, the danger to life lies in the development of dehydration.

CHAPTER 6

PREVENTION OF MORTALITY AND MORBIDITY IN INFANCY

"Learn before thou speak, and use physick or ever thou be sick".

Apocrypha: Ecclesiasticus 18,19

PREAMBLE

The promotion and maintenance of health and the prevention of disease should be the aim of any medical service and of all individual doctors.

"The primary reason for studying the dead is to save the living" (Potter, 1961); the analysis of the causes of death in Chapters 1 - 3 and the discussions in Chapters 4 - 5 pave the way for consideration of where we stand at present in the important field of preventive paediatrics and along which lines advances may be expected in the future. The aim of this Chapter is to discuss prevention, not specific treatment. Even then, the field is a vast one and discussion will be restricted mainly to the causes of mortality and morbidity highlighted in previous Chapters.

The birth of a live, healthy baby is not the culmination of a comparatively short labour, not the culmination of nine months of pregnancy, but the result of the interplay of a host of factors including genetic inheritance, the mother's own health from birth to maturity, the foetal environment, which includes the mother's health during pregnancy, and the quality of antenatal and intranatal medical and nursing care.

PART 1 THE POTENTIAL MOTHER

Factors underlying the maintenance of health of a community are to a large extent now understood. The biological sciences have progressed markedly in the last century and the two major problems in the general health of a population, control of communicable disease and the aetiology and prevention of nutritional disorders, can be regarded as largely solved.

What is still lacking in many parts of the world is the application of this knowledge (WHO, 1968). This is particularly so in the "underdeveloped" countries; the influence of poor standards of general health on the infant population is reflected by infant mortality rates in some areas of over 200 per 1000 births.

Socio-economic circumstances. In this country regional differences in peri-natal mortality in the past were ascribed to the effects of socio-economic circumstances, high perinatal and infant mortality figures being associated with poverty, unskilled occupations and large families (Baird, 1969). A number of factors could be incriminated, such as the general effects of malnutrition on height and skeletal development, and ignorance leading to failure to make use of welfare and medical facilities available. In the past 25 years, however, these regional differences have become very much less marked as there has been a gradual overall improvement in the national state of nutrition and health. Nevertheless, Butler and Alberman (1969) still consider that many of the present generation of mothers are not as healthy and well grown as they should be.

In the developed countries, in general, the potential mother should reach the age of reproduction in a fit physical state; child clinics, school medical services, welfare facilities and general practitioner and hospital services are freely available to all in this country. Although improvement in general health has been marked in this century, continued propaganda is required to ensure that facilities available are fully utilised. In the developing countries gradual improvement in communal health is being made by the efforts of aid schemes and the activities of the World Health Organisation and allied bodies.

Maternal age. Crosse and MacIntosh (1954) analysed the relationship between maternal age and infant mortality, their figures are reproduced in Table XXXI.

	Maternal age in years					
	Less than 20	20-24	25-29	30-34	35-39	Over 39
Number of births	387	2772	3622	2076	972	119
% death rate	1.8	2.7	2.7	3.9	6.3	8.6

Table XXXI. Maternal age and infant mortality

(after Crosse and MacIntosh 1954).

There is a slight increase in infant loss up to the maternal age of 30, but a marked increase occurs from the age 35 onwards. Increasing age is an adverse factor in the incidence of toxaemia of pregnancy, unexplained premature births, unexplained death in mature foetuses and mechanical complications during labour (Butler and Alberman, 1969). Physiological efficiency as regards reproduction appears to be at a peak at the ages of 18-20.

Parity. The first pregnancy carries greater hazards than the next two of three, as the primipara is more likely to develop pre-eclampsia and have a difficult labour, thereafter the hazard increases steadily with increasing parity, the incidence of conditions peculiar to pregnancy, premature live births and stillborn and neonatal death rates all being higher in the grand multipara than in earlier pregnancies. (Russell and Thompson, 1970).

Previous obstetric history. Women with a history of complications in previous pregnancies are at greater risk of further difficulties if they again become pregnant (Russell and Thompson, 1970). The foetus in such cases, therefore, is more at risk.

Smoking. In the Perinatal Mortality Survey, Butler and Alberman(1969) showed that the mean birth-weight of infants born to women who smoked was 170 g lower than in those born to non-smokers and stillbirth rates were some 40% higher in the former category.

Genetic Counselling. Sufficient is now known about diseases mediated by chromosomal and gene defects to allow the commencement of genetic counselling. At present the scope of this is such that only a small proportion of the population can benefit and advice is generally confined to assessment of the risk of recurrence of a congenital defect if siblings of an affected child are conceived. (WHO, 1969b). The science of cytogenetics is still in its infancy and the future will almost certainly see a considerable widening of the scope of genetic counselling; pre-marital advice based on cytogenetic and family studies may lower the incidence of a number of diseases, such as the haemoglobinopathies.

Rubella. The recognition of the rubella syndrome has led to the development of an effective rubella vaccine, and if adequate propaganda leads to all potential mothers being protected, the tragedies of major and minor disabilities due to rubella infection of the foetus in utero should be greatly reduced.

PART 2. THE FATHER

The socio-economic state of a family is largely dependent on the father's position and a low state is reflected in the general physical state and nutrition of the mother. Although poor health standards should not occur in this country, they still do; governmental and local authority action is gradually overcoming adverse problems in the environment by such measures as slum clearance, social security benefits and raising of living standards. These should bear fruit, as they have in the past, and it appears a fair comment that each successive generation in this country enjoys a higher socio-economic position.

The genetic contribution to the conceptus by the father may determine hereditary disease. A raised paternal age seems to be a factor in a small proportion of infant malformations, for example osteogenesis imperfecta, suggesting that gene mutation may have occurred (Butler and Alberman, 1969).

PART 3. THE PREGNANT WOMAN AND THE CONCEPTUS

A. General considerations

The pregnant woman and her conceptus cannot be discussed separately as so many factors which influence one affect the other.

The essence of ensuring that an expectant mother and her unborn infant are carried through the pregnancy to labour in the optimum condition is the quality of antenatal care. In the developed countries facilities for antenatal care are available for all pregnant women, but full use of them is not always made and in some cases the quality of such care leaves much to be desired.

Butler and Bonham(1963), in stressing the importance of early antenatal attendance, by the 16th week of pregnancy at the latest, recorded that less than half (48.8%) of all expectant mothers did so report. Whereas 56.4% of women expecting their first child commenced antenatal care at or before this time, the percentage fell considerably among parous women, to a figure of only 29.5% attending antenatal clinics before the 16th week in the case of fifth or subsequent pregnancies. This failure to take advantage of the health services available can only be countered by propaganda and this constitutes a major contribution which could be made in the field of preventive paediatrics. In this era when mass communication is available to practically every household, particularly through television, opportunities exist for effective health propaganda, but are seldom utilised.

Butler and Bonham also quoted figures reflecting the quality of antenatal care. The frequency of some routine examinations in various types of clinics are reproduced in Table XXXII.

Type of clinic	No haemoglobin estimation	No blood pressure estimation	No Rh grouping performed
Hospital	4.7	1.6	0.7
General practice	60.0	17.8	12.0
General practice + midwives	67.9	25.4	13.0
All clinics	33.3	15.9	5.5

Table XXXII. Failure (in percentages of population attending) to carry out certain examinations in various types of antenatal clinics

(After Butler and Bonham 1963)

As the effects of anaemia, hypertension or rhesus iso-immunisation need no stressing, this Table is a sad reflection on some medical services.

Baird (1969) has stressed the importance of the quality and training of doctors and midwives in relation to the prevention of perinatal mortality; a second major contribution which could be made to the prevention of morbidity and mortality is in this field, the province of medical schools and the Royal Colleges.

The object of antenatal care is the promotion (not only maintenance) of maternal health, the early diagnosis and treatment of intercurrent disease and of conditions peculiar to pregnancy, and careful assessment of the progress of the conceptus and of the influences of factors potentially inimical to it.

B. Intercurrent Disease

Apart from stressing the importance of the general health of the mother, the prompt diagnosis and treatment of maternal infections (especially renal and venereal), the recognition and treatment of systemic disorders (such as anaemia and diabetes), the general subject of incidental and intercurrent disease in pregnancy need not be elaborated here. Their management may have a profound effect on the progress of the pregnancy and the outcome of labour; a high degree of medical and nursing care of general problems provides an important contribution to the outcome of a pregnancy.

The attainment of this high professional standard depends on the quality of undergraduate and post-graduate medical education and the quality of nurse training.

Intercurrent disease such as rubella infection may have more specific effects on the foetus.

C. Conditions peculiar to pregnancy

i. Toxaemia

Despite intensive research for many years, little is known about the cause of one of the most important complications of pregnancy as regards perinatal mortality, pre-eclamptic toxaemia and eclampsia itself. Johnstone and Keller (1968) have described this condition as "the disease of theories", but admit that nothing is known about its aetiology.

At present it is responsible for 12.6% of perinatal deaths (Butler and Alberman, 1969). These authors record the incidence of this condition as occurring in a mild form in 17.4% of all pregnancies, in a moderately severe form in 4% and in a severe form in 6.1%. The perinatal loss from pre-eclamptic toxaemia and eclampsia is of the order of 5% in mild cases, 10% in moderately severe cases showing the triad of hypertension, oedema and albuminuria and 25-30% in severe cases having a blood pressure over 180/110 and more than five g of albumin per litre of urine. (Johnstone and Kellar, 1968). The risk to the infant lies in unexplained death in utero, delivery in a state of acute asphyxia or premature delivery.

Understanding of the cause of toxaemia in pregnancy and its prevention would be a major advance in lowering the incidence of maternal morbidity and perinatal infant mortality. In the meantime, empirical management involving careful antenatal supervision and induction of labour when indicated is very effective in practically abolishing eclampsia and greatly reducing the incidence of severe pre-eclampsia (Russell and Thompson, 1970).

ii. Antepartum haemorrhage

Antepartum haemorrhage accounted for 14.2% of perinatal deaths in the British Perinatal Mortality Survey (Butler and Alberman, 1969). Accidental haemorrhage may follow separation of a normally positioned placenta (abruptio placenta) or of one in an abnormal place (placenta praevia). In the case of the former, hypertension or folic acid deficiency may be the cause and attention to these arising in pregnancy are obvious prophylactic measures. Baird (1969) reported a striking reduction in the incidence of abruptio placenta when haemoglobin estimation was carried out at every antenatal examination and treatment of anaemia instituted if indicated. Nothing is known as yet of the causes of placenta praevia and all that can be done to reduce its dangers are early diagnosis and skilled clinical judgement in management. Considerable advances have been made in recent years in localisation of the placenta by radiography, including aortography and radioisotope techniques, ultrasonic devices and thermography (Russell, 1970), but until the cause of placental malposition is discovered no specific measures to prevent it can be taken.

D. Other maternal/foetal factors

Careful antenatal supervision should lead to the recognition of a variety of other factors which may be amenable to the "skills and manoevres" of the obstetrician and his colleagues (Chamberlain, 1970), and hence help to prevent perinatal morbidity and mortality. These include cephalo-pelvic disporportion, malpresentations and malpositions of the foetus, multiple pregnancies, "small-for-dates" babies and post-maturity.

The true premature baby, having a low birth weight because of a shortened gestation period, can only be diagnosed in retrospect at birth, but the foetus with a lower weight than it should have for its gestational period, the "small-for-dates" or dysmaturic baby, can be diagnosed in

utero with reasonable certainty (Loeffler, 1967). The dysmaturic baby has suffered from intrauterine retardation due to placental insufficiency, maternal toxaemia or early intrauterine bleeding, or hypoplasia due to malformation or infection (Maclaurin, 1970). At present little can be done to prevent such a situation arising, but the recognition of a dysmature infant before labour can alert the obstetrical staff to the need for special care.

The incidence of cephalo-pelvic disproportion is low in mothers who have been well nourished throughout their life and improvement in socio-economic circumstances is the essential preventive measure.

Perinatal mortality from the other factors listed, and in cases of cephalo-pelvic disproportion which do arise, can be largely prevented by clinical diagnosis and wise management.

F. Factors directly inimical to the conceptus

Maternal disease, incidental or peculiar to pregnancy, and miscellaneous maternal/foetal factors may lead to a situation in which the foetus is in the chronic high risk group as regards the outcome of pregnancy and labour. A number of factors may operate more directly on the conceptus, the main conditions resulting being congenital malformations and erythroblastosis foetalis.

Congenital malformations

The state of knowledge concerning the aetiology of congenital malformations has been discussed in Chapter 5. Foetal diseases may be genetically determined or arise from environmental factors, or both, but in only a minority of cases, as yet, can the cause be pin-pointed. Research has enabled progress in prevention, or in prevention of sequelae, in a number of conditions. The progress in this field has been impressive in the past three decades and another major contribution which can be made to preventive paediatrics is continued research.

In the field of cytogenetics the value likely to result from genetic counselling has been mentioned. Progress in cytogenetics has not yet enabled much advance in true prevention, but such procedures as amniocentesis and chromosomal studies of foetal cells about the 14th week of pregnancy may enable prediction of a major handicap so that therapeutic abortion may be considered.

Apart from such limited procedures, the anatomical or metabolic defects resulting from congenital malformation are, speaking generally, not evident until after birth and much of the discussion on the prevention of morbidity and mortality from these conditions will be deferred until the neonate and infant are considered. In this Part, consideration should be given to environmental factors adverse to the foetus which intimately concern the pregnant woman, chiefly potentially teratogenic agents amongst which drugs, radiation and some infections are the most important.

The role of many drugs in the development of foetal abnormalities is still debatable. At a recent medical conference held by the US Army in Europe, a speaker circulated a list of 53 drugs which had been reported to affect the foetus or neonate in some way, ranging from the production of malformations to haematological effects and depression of respiration (G C Glenn, personal communication). Nora et al (1967) carried out a prospective study on 240 mothers as regards exposure to drugs and other factors which were potentially teratogenic and found that in the first trimester of pregnancy there was a mean exposure to no less than 3.1 drugs which could be harmful. During the entire pregnancies the mean exposure was to 5.4 drugs. Although there was no statistical difference between the number of babies with malformations whose mothers were exposed to potentially teratogenic drugs in the first trimester compared with those not taking drugs during this period, the authors considered that as many abnormalities have a multifactorial aetiology, teratogens

might precipitate their development in individuals possessing a hereditary predisposition to malformations. The majority of the drugs were prescribed by physicians and not instances of self-medication; a severe criticism of the lack of attention paid to the lesson of the recent thalidomide tragedies. The great majority of the drugs prescribed were considered unnecessary, an example being the prescribing of antibiotic drugs for respiratory infections which were probably viral in origin.

Until the influence of drugs on the foetus is better understood, it would appear rational to restrict exposure of pregnant women to them, prescribing drugs only on clear clinical grounds.

Radiation is another potential teratogenic agent. Stewart et al (1956) conducted an environmental survey of some 1500 children dying of malignant disease, including leukaemia, before the age of ten years. Controls of live children of the same age, sex and locality were chosen at random. Among the findings was that the number of mothers who had radiological examination of the abdomen during pregnancy was 85% for the malignant disease cases, 45% in the control group. Kaplan (1958) reviewed the somatic and genetic hazards of the medical use of radiation. He considered that the evidence of the hazard of radiological pelvimetry in the production of leukaemia was unconvincing. Radiation has been proved to cause gene mutation in lower animals and in plant life. This was independent of dose-rate, that is, there was no threshold dose below which no effect will occur, and he concluded that mutagenic effects could occur in the human and hence exposure of a foetus to diagnostic radiology should be kept to a minimum. MacMahon (1962) conducted a survey of a 1% sample of a population of 732,343 children and estimated that mortality from cancer was about 40% higher in infants exposed in utero to diagnostic doses of radiation than in those not exposed.

Modern radiological techniques, however, have led to a substantial lowering of the dose of radiation in diagnostic work, so that the figures quoted, based on children born in 1947-53, probably exaggerate the risk nowadays (Russell 1970).

Radiation of the foetus in diagnostic doses may carry the hazard of inducing malignant disease or gene mutation; these hazards must be balanced against the hazards of delivery if a condition inimical to the foetus, which could have been diagnosed radiologically, is missed. Certainly in the light of present knowledge radiological examination of the pregnant uterus should only be carried out where there are convincing clinical grounds.

At present three teratogenic infections have been recognised. The importance of an energetic campaign to ensure that all prospective mothers are immunised against rubella if they have not suffered from the natural disease has been mentioned. The value of immunoglobin in the prevention of rubella in those exposed to infection is debatable and active immunity should be the goal. Infections with cytomegalus virus and toxoplasma gondii are frequently sub-clinical in adults and at present there appears little that can be done in preventing foetal infection by these agents. Research may incriminate further teratogenic infection (White and Sever, 1967) which may be amenable to prevention.

Erythroblastosis foetalis

As long ago as 1943, Levine pointed out that in matings where parents were incompatible as regards the ABO blood group there was a lower incidence of haemolytic disease of the newborn than where the parents were ABO-compatible. The assumption that this was due to ABO-incompatible foetal cells being destroyed in the maternal circulation by the mother's natural anti-A or anti-B antibodies before they could immunise the mother against Rh antigen was confirmed by Stern et al(1956)

who found that if Rh positive red cells were injected into Rh negative males, the anti-D titre resulting was much higher when compatible ABO blood was injected than when incompatible ABO cells were used.

These findings led the Liverpool School (Clarke, 1967) to a brilliant deduction and important advance in preventive paediatrics. They considered that if an Rh negative mother, pregnant with an Rh positive foetus, was given anti-D antibody after delivery, any Rh positive foetal cells in the maternal circulation would be destroyed before there was time to stimulate maternal sensitisation. Clinical trials amply confirmed this deduction, which had also been pursued independently in other countries.

Anti-D immunoglobulin injected within 60 hours of delivery into Rh negative mothers who have given birth to an Rh positive, ABO compatible baby, and whose blood shows the presence of foetal red cells, almost always prevents the development of Rh immunisation.

In a review (Clarke 1967) of controlled trials in such primiparous women, 75 out of 559 control patients not given Anti-D immunoglobulin developed active immunity, with Rh antibodies in their serum, six months after delivery, whereas only one woman in 628 patients protected with Anti-D showed active immunisation. Records from 118 dependents of Army personnel given Anti-D in like circumstances show that none had Rh antibodies six months after treatment.

There have been occasional failures reported, but the overall efficiency of this treatment has led it to be accepted for routine use in this country.

While erythroblastosis foetalis will still occur in babies of women already immunised against Rh antigen (this will decline over this generation), from occasional failure of the prophylactic injection of Anti-D immunoglobulin and from cases of ABO and the rarer blood group

incompatibilities, the incidence of this condition should be greatly reduced.

This work constitutes one of the more satisfying chapters in the prevention of foetal mortality and neonatal morbidity and mortality.

G. Recognition of the high risk foetus

The discussion so far enables recognition of pregnancies where the foetus may be at high risk in its intrauterine environment or at delivery. In contrast to the acute hazards which may arise during labour, these may be designated chronic risks.

The major causes of a chronic high risk situation may be recapitulated as follows:-

Factors affecting the potential mother	Socio-economic circumstances Age Parity Previous obstetric history
Factors affecting the pregnant woman and the conceptus	Intercurrent disease including: Infections Anaemia Diabetes Conditions peculiar to pregnancy: Toxaemia Antepartum haemorrhage Other maternal/foetal factors: Cephalo-pelvic disproportion Malpresentations and malpositions Dysmaturity Post-maturity Smoking

Factors directly inimical to the conceptus	Congenital malformations
	Genetic make-up of both parents
	Environmental teratogenic agents including:
	Drugs
	Radiation
	Infections
	Blood Group incompatibility.

Primary chronic risks arising from an adverse socio-economic environment throughout the prospective mother's life can, in the long term, be prevented by improvement in communal health. Secondary risks arising from maternal age and parity or from complications arising during pregnancy, can, in some instances, be minimised or prevented by prompt recognition and treatment of these conditions; in many cases, however, knowledge is as yet insufficient to prevent or cure such complications and it is in this area that the quality of antenatal care leading to the appreciation of a high risk situation is of fundamental importance in the preservation of foetal life.

Technical aids to the clinical assessment in antenatal care are increasing and have been reviewed in a recent volume of the British Journal of Hospital Medicine. Apart from normal support from pathology laboratories in routine haematological, bacteriological and biochemical investigations of the mother, advances of a more sophisticated nature are gradually being introduced. Ultrasound techniques and amniocentesis with biochemical and cytological examination of liquor amnii aids in the estimation of foetal growth and development (Lind, 1970). Amnioscopy may enable early detection of the foetus likely to be at risk during labour (Henry, 1970). The estimation of a number of biochemical parameters in blood obtained from the scalp of the foetus while still in

utero may enable a more precise estimate of its condition (Beard, 1970). Many studies have demonstrated the value of oestriol assay in the mother's urine in the diagnosis and management of complications of pregnancy, particularly the development of that ill-understood condition of placental insufficiency (Turnbull, 1970).

Such advances are in the diagnostic field and do nothing to prevent complications arising, but the diagnosis, and hence the management, of these conditions will lead to reduction in perinatal morbidity and mortality.

PART 4. DELIVERY AND THE NEONATE

As the immediate progress of a newly-born infant is largely determined by its experience during labour, delivery and the neonate must be considered together. The discussion in this Part will be restricted to conditions peculiar to the neonate, the more general causes of morbidity and mortality arising during neonatal or infant life, such as congenital disease, accidents and specific infections, will be dealt with when the Infant is considered.

To the chronic risk situation already discussed, two further major factors, an acute risk situation and premature delivery, may now be added.

Acute risk situations. There is a physiological degree of foetal hypoxia in normal childbirth, but this may be added to, and produce a dangerous situation, by a number of conditions, the more important of which are:

a. Uterine factors. Hypertonia of the mymometrium, a prolonged second stage or premature separation of the placenta can lead to a diminished oxygen transfer to the foetus.

b. Umbilical cord factors. Compression of the cord, including by prolapse, can virtually cut off the oxygen supply to the foetus and lead to acute anoxia and death; lesser degrees of

interference can accentuate the normal hypoxia.

c. Foetal/neonatal factors. Depression of the respiratory centre leading to diminished pulmonary exchange in the immediate post-partum period can result from trauma due to a complicated delivery or from the effects of drugs given to the mother.

Premature delivery. The reasons why labour should commence before the full gestational age of the foetus has been reached are obscure. The underlying factor is often that of a chronic risk situation, premature labour frequently being associated with uterine abnormalities, multiple pregnancies, toxaemia and general maternal ill-health, but a certain number occur without any known precipitating factors.

It is evident that the prevention of perinatal morbidity or mortality arising from acute or chronic risks largely depends on the judgement of the clinical situation and this depends on the quality of obstetrician and midwife care. Administrative and technical facilities can contribute to professional expertise.

Arrangements for lying-in. I once heard an obstetrician remark that "no labour is normal except in retrospect" and this should be the keynote in the provision of facilities for delivery. It demands that domiciliary confinement should have no place in modern obstetrical practice, yet Butler and Bonham (1963) recorded that only 40.9% of the population was booked and delivered in fully equipped hospitals; the fact that 23% of nulliparous females booked for home delivery had to be transferred to hospital underlines the risk to which domiciliary delivery may expose both mother and foetus. Baird (1969) discussed the evolution of maternity services in the City of Aberdeen over the past 20 years. In 1945 only 45% of women in that city booked for hospital confinement, by 1967 almost 100% were confined in hospital under the care of specialist obstetric and paediatric staff. Perinatal mortality fell from 46 per 1000 live births

in 1946-48 to 24 in 1944-46 and Baird concluded that the majority of deaths preventable by technical skill had been eliminated.

The standards attained in Aberdeen could be reached elsewhere by modernisation of the maternity services so that facilities are available for all confinements to take place in fully-equipped hospitals.

Intensive care. The time-honoured practice of monitoring the condition of the foetus by recording the heart rate by means of a foetal stethescope only indicates the rate between uterine contractions, but the stress of these contractions may not be evident if auscultation is only possible in the inter-contraction period (BMJ 1971a). Methods of continual monitoring of the foetal heart and determination of the pH of the foetal blood are now available (Pendleton, 1970; Beard, 1970) and provide a reliable indication of the condition of the foetus, on which information important decisions as to immediate management - the necessity for operative delivery for example - can be taken. The universal introduction of such foetal monitoring for all patients in labour presents formidable problems in staffing and finance, but when more experience in new techniques is gained it is probable that these sophisticated methods will have a much wider application than at present, aiding the obstetrician and midwife to arrive at a more precise assessment of the condition of the foetus during labour and hence indicate the necessity or otherwise for active interference.

The keynotes in the prevention of infant morbidity and mortality from the major conditions peculiar to the neonate discussed in Chapters I and 5, are the quality of professional care, antenatally and intranatally, and the provision of adequate facilities.

Birth trauma arises from mechanical factors. Most of the conditions which predispose or lead directly to it are in the chronic high risk group. Cephalo-pelvic disproportion, malpositions and malpresentations

and post-maturity should all be detected during adequate antenatal supervision and appropriate steps taken before or during labour to counteract them. The dangers of an acute risk situation resulting from precipitate labour or a prolonged second stage can be minimised by adequate training and lying-in facilities. Chamberlain (1970) stated that intracranial trauma is less often seen nowadays, "the grimm determination to achieve vaginal delivery being a thing of the past".

Neonatal asphyxia and the respiratory distress syndrome have much in common aetiologically. Very many factors, often in combination, can lead to respiratory depression immediately after birth or in the subsequent few days. The cause of some can be pinpointed, but much still remains to be discovered about the reasons why some babies are born prematurely and the factors underlying the cause of "small for dates" babies. The possible role of the lack of surfactant causing the respiratory distress syndrome has been discussed, but continued research is required into this major cause of infant mortality. Until more understanding of these factors permits prevention, much can be done, as in the case of birth trauma, by antenatal recognition of the high risk factors and the amelioration or remedy of such risks as far as possible. As discussed in Chapter 1 (page 29) in a number of cases of respiratory depression in which the pathological findings and the neonatal clinical course closely parallel the findings of those recognised as being in the high risk group, no adverse maternal, labour or foetal factors may be evident. This situation reinforces the importance of hospital confinement where the unexpected asphyxiated infant, or one in whom respiratory distress develops after an interval, may have immediate expert attention from the obstetrician/paediatrician team.

Rhesus haemolytic disease and the means of prevention by anti-D immunisation of Rh negative mothers giving birth to Rh positive infants

have already been discussed (Page 159). Cases may still arise in babies of women already immunised against the Rh antigen, occasional failure of the prophylactic injection of Anti-D immunoglobulin and from cases of ABO and the rarer blood group incompatibilities. Such measures as foetal transfusion (Liley, 1963; Bowman et al, 1969), early induction of labour and exchange transfusion shortly after birth may prevent mortality and morbidity from the major sequalae of this condition, severe haemolytic anaemia and kernicterus.

Infections peculiar to the neonate involving a possible fatal outcome are mainly umbilical sepsis and pneumonia. Prevention of the former depends on nursing care and is an uncommon complication. In the early days of life pneumonia generally affects lungs in which the alveoli are abnormal as a result of birth stress, such as atelectasis resulting from respiratory depression due to severe asphyxia or a water-logged state due to excessive aspiration of liquor amnii often seen in anoxic states (Macgregor, 1947). Infection occurs from the foetal environment and is generally bacterial. Prevention of neonatal pneumonia of this type follows the same principles as underly the prevention of neonatal asphyxia discussed above.

PART 5. THE INFANT

In this Part the major conditions producing morbidity and mortality in the infant below the age of two years, including the neonatal period for diseases not peculiar to the neonate, will be considered.

Table XVIII showed that 18.4% of deaths in my series of cases were due to infections leading to serious illness, 23.2% were unexpected deaths deemed to be largely due to fulminant infections, 15.2% were due to congenital malformations and 4% were the result of accidents.

A. Infective conditions.

The striking fall in deaths from acute specific infectious diseases during the first year of life, from 10,196 in 1900 to 58 in 1960 in this country (Table XXI), and the associated fall in morbidity which must be even more impressive, together probably form the most significant achievement in medicine in this century. The preventive methods bringing about this achievement are improvements in public health in its varied aspects, immunisation and chemotherapy. Table XXI shows that the fall in incidence of the acute fevers has been progressive since 1900 and indicates that the main factor is in the public health field as the other two factors are of more recent origin. Better accommodation, stricter control over food and water supplies and of waste disposal are the chief areas in which improvement has occurred in this context. Such measures, by decreasing exposure to disease eventually produces a more susceptible population who have not become naturally immunised by overt disease or repeated sub-clinical infection. Hence the paramount importance nowadays of artificial active immunisation as a means of preventing epidemics should infection be introduced into a community. The campaigns conducted to immunise the infant against whooping cough, diphtheria and poliomyelitis have, in conjunction with public health measures, virtually eliminated these diseases, but it is imperative that the absence of these diseases should not lead to complacency and a decline in those being immunised; disastrous epidemic situations could arise in that event.

The recent introduction of a measles vaccine should in time, if an energetic campaign for immunisation is pursued, lead to the practical elimination of this disease, a cause of much infantile morbidity.

Progress has been equally striking in the prevention of the chronic specific infectious diseases such as tuberculosis and syphilis in infancy. Improvements in the environment, including elimination of tuberculous

cattle, and in nutrition, have lowered the incidence of tuberculosis remarkably. In the last two decades BCG vaccination of older age groups and potent chemotherapeutic agents, by further decreasing the overall incidence of the disease, have decreased the exposure of infants to infection. Routine serological tests for syphilis at antenatal examination has virtually eliminated cases of congenital syphilis.

The picture is different, however, when one considers respiratory and intestinal infections. Although mortality has decreased very considerably since the beginning of this century, less than 3000 infants dying from respiratory disease in 1960 compared with over 24,000 in 1900, there is still a considerable infant loss. Many of these infections are primarily viral in origin and, until methods of eliminating respiratory viruses from the community by immunological or chemotherapeutic measures are discovered, little hope can be held out that these figures will be substantially reduced. This is another field where continued research may provide the answer.

Intestinal infection in infancy has changed in pattern over the past 70 years and although the incidence of this condition is still very considerable, probably some 100,000 cases a year, the mortablity is very much less owing to changes in the bacteriological agents and advances in treatment. The disease is mainly sporadic, with occasional institutional outbreaks. Education of families in personal hygiene, and prompt action when cases occur in an institution, will further decrease morbidity and mortablity. The danger to life lies mainly in the development of dehydration and education of the medical profession in the prompt recognition and treatment of this complication could save many lives.

Although the prevention of respiratory and intestinal disease in infancy does not appear to be possible as yet, this question of the education of the medical profession has a considerable bearing on the

possible outcome. Selwyn et al (1965) analysed the causes of 184 deaths in infancy. 40 were due to primary infection. The most significant observation was that over one-half of the deaths of a non-fulminant nature (23) could have been prevented if delay in instituting appropriate treatment had not taken place. The authors judged that 6 of these deaths were due to parental negligence in not summoning medical aid and the remaining 17 were due to a failure to arrive at a clinical diagnosis or the giving of inadequate treatment. Even some fulminating cases of infection could have been saved by prompt, energetic therapy. It was considered that junior medical staffs in hospital were often not aware of the rapidity with which acute infections could kill children, echoing the views of Bowden (1950) quoted in earlier Chapters.

This article reflects the importance of the quality of professional education, pre- and post-graduate, which is a recurrent theme throughout the whole of this chapter.

B. Sudden or Unexpected Death in Infancy

The conclusions reached in Chapter 4, that most cases of sudden or unexpected death in infancy was due to fulminant infection, predominantly respiratory, carries little hope for preventive measures until methods of eliminating respiratory viruses from the community are available. Frequently cases of this nature do have minor symptoms which on occasion lead parents to seek medical advice, but physical examination is generally negative and there is no indication that a fatal outcome might ensue. Indeed minor symptoms are widespread in the infant population and in most cases are in actual fact trivial, so that there is little hope that the presence of these will lead to preventive measures which in the vast majority of cases are not indicated. The possibility of underlying biochemical defects in cases of sudden or unexpected death in infancy has

been mentioned; even though these may not play a part, certainly more work in paediatric chemical physiology and pathology is required.

C. Congenital Malformations

The part played by genetic inheritance and adverse factors in the foetal environment in the production of congenital malformation has already been discussed, and measures such as genetic counselling, protection of the foetus by avoidance of radiation and unnecessary or teratogenic drugs in pregnancy, and prevention of maternal rubella by immunisation have been mentioned.

Much research remains to be done on the basic causes of congenital malformations and studies of affected infants, including their family and intra-uterine experience, are important tools in the investigators' hands. The effects of environmental factors is ill-understood, but such investigations could well produce fruitful results. As an example, it has been well established from study of infant populations that there are marked ethnic differences in the incidence of central nervous system anomalies such as anencephaly and spina bifida. In Boston, USA, the rate is recorded as 3.1 per thousand babies born to parents of Irish ancestry, but the offspring of Jewish mothers have an incidence of 0.77 per thousand (Naggan and MacMahon, 1967). Considerable variations in the incidence of spina bifida in Northern Ireland, Wales, Scotland and England, have been documented (BMJ, 1969b). Evidence of this nature strongly suggests that such conditions are of an environmental nature and not of genetic origin. If this is so, and the environmental factors can be discovered, the future as regards prevention of these conditions holds out hope.

Until the many research projects in hand in many centres throw more light on the aetiology of congenital defects, true prevention is only possible in a minority of cases, but much can be done to prevent or

ameliorate mortality and morbidity in those affected.

Congenital malformations can be manifested by structural anomalies or by metabolic defects leading to serious sequelae.

Advances in radiological, anaesthetic and surgical techniques have enabled more precise diagnosis and remediable surgical operations to be undertaken in many cases of anatomical defect. The application of these to severe congenital heart disease has been reviewed recently (BMJ, 1971b). In one centre the overall survival rate increased from 27% in the period 1962-65 to 51% in 1966-69; a striking improvement was particularly evident in cases of hypoplasia of the right heart and transposition of the great vessels, the survival rate raising from 9% in the first period to 64% in the second. This leader also drew attention to the mistaken belief that cardiac surgery is badly borne by the neonate; diagnosis and operative interference at an early stage before cardiac decompensation has occurred has a profound effect on prognosis. Appreciation of the need for referral of such cases rests on the team first responsible for the baby's welfare - the midwife, general practitioner, obstetrician and paediatrician. Similarly early diagnosis with appropriate surgical intervention is essential in many of the other rarer, but often lethal, congenital malformations resulting in atresia or stenosis in various sites.

Inborn errors of metabolism arising from congenital defect are numerous. Although their prevention is not yet possible, early recognition of the defect may enable steps to be taken to prevent or minimise their effects. Many are due to the absence of specific enzymes which lead to the absence of the product for which the enzyme is required, such as the absence of A haemoglobin in thalassaemia or of insulin in some types of diabetes. Lack of a specific enzyme may lead to the substrate on which it should work accumulating in the body, such as occurs in phenylketonuria, or it may lead to an alteration in the metabolic pathway,

with normal metabolites accumulating in the body or being excreted in unusual quantities, such as is seen in leucinosis (maple syrup disease).

Steps which are possible at present to ameliorate the sequelae of diseases of this nature are to supply the missing enzyme, for example insulin in the treatment of diabetes, or in dietetic control such as a phenylalanine - free diet in phenylketonuria. Early diagnosis is essential in many of these conditions so that treatment may be initiated before irreversible damage has taken place. For example, the detection and treatment of phenylketonuria early in infancy can prevent severe and permanent intellectual impairment (BMJ, 1968c). Mass screening of neonates about the sixth day of life for this conditions is now carried out in many centres. Such screening could be extended to search for other inborn errors of metabolism as techniques for simple detection are evolved.

In the future further advances may permit other metabolic conditions to be treated. For instance when the science of immunology has advanced sufficiently to prevent transplant rejection,it may be feasible to replace the bone marrow in sickle cell anaemia or in beta-thalassaemia. In the long term, if the present impetus of research in cytogenetics is maintained, radical treatment of a number of these conditions may be achie achieved (WHO, 1970).

D. Accidents

Accidents, including poisoning, are a major cause of death after the first year of life and constitute a challenging field for preventive measures (Nelson, 1964c). Nelson quotes some staggering figures for the USA - 15,000 children below the age of 15 die yearly as a result of accidents, 50,000 are crippled and some 2 million are incapacitated for some time; these accidents arelargely preventable. As regards the infant below the age of 2 years, the main danger period is during the second year when he commences to walk. The child's instinct for exploration may

lead him into dangerous situations, falls, drowning, scalds and burns being the main cause of accidental death in this period. Preventive measures seem obvious; the design of cots and safeguards in the house, guarding sources of heat, keeping drugs out of reach and a commonsense approach to the latitude given to the infant, so that dangerous situations are avoided, but undue restraint is not exercised, to allow experience to be gained. The toll of child life from accidental causes, however, indicates the apathy with which many of these measures are treated; it requires much more effort in the way of education of parents in simple elementary precautions and this would be a most suitable and rewarding subject for propaganda by means of the mass media available nowadays.

PART 6. PREVENTIVE PAEDIATRICS: RECAPITULATION

Notable advances in medicine have taken place during this century and have been reflected in the outstanding improvement recorded in infant mortality and morbidity in the developed countries. Clinical and laboratory research has led to such important contributions as nutritional requirements, elucidation of the pathogenesis of many important medical conditions including the effects of iso-immunisation and the aetiology of a number of inborn errors of metabolism, a greater understanding, though far from complete, of human genetics and the control of infective disease by chemotherapy and immunisation. Previous parts of this chapter have discussed the present position of preventive paediatrics and the fields in which important gaps in our knowledge still exist. In this concluding part the general factors which will further improve infant health will be summarised.

The standard of professional care has been mentioned frequently. The overall competence of the medical and nursing professions and ancillary professions supplementary to medicine in this country is not questioned, but there is always room for improvement at group and

individual levels. Increasing vigilance by medical schools, the Royal Colleges and the Nursing Councils to maintain and improve the standard of student and post-graduate training will do much to decrease infant mortality and morbidity. At governmental level implementation of proposals advanced by the Royal Commission on Post-Graduate education (Todd 1968) would raise professional standards.

These standards affect the whole spectrum of health, but in the context of the infant are particularly relevant in the antenatal period, at the time of delivery and at post-natal examination. Antenatal care includes the promotion of maternal health, the early diagnosis and treatment of intercurrent disease and of conditions peculiar to pregnancy and assessment of the progress of the conceptus so that the chronic high risk case may be recognised early. The keynotes at the time of delivery are early diagnosis of an acute risk situation and wise management. Prompt physical examination and observation of the neonate will detect acquired illness and remediable congenital disease, the management of which can prevent serious disability in the future life of the infant.

Continued research is required to close the many gaps which still exist in medical knowledge. Notable among these in the present context are the cause of many types of congenital malformation, the aetiology of a number of conditions peculiar to pregnancy, the mechanism of respiratory distress in the newborn and the prevention of acute respiratory disease of viral origin in the infant.

Community health programmes of a high order are essential if professional care is to be properly exercised. Infant mortality and morbidity is greatly influenced by socio-economic circumstances and improvements which have taken place, and should continue to take place, in housing, nutrition and the general environment will bear fruit. Antenatal supervision is one of the most important aspects of the maternity services and proper facilities should be available in health centres or out-patients

departments. Facilities for delivery in large, properly equipped and staffed hospitals should be available for all pregnant women and these facilities should include intensive care units and laboratory support for modern aids to foetal monitoring.

An important contribution can be made by the application of existing knowledge through education and health propaganda measures. Instruction in the physiology of human reproduction, nutrition and hygiene should promote optimal maternal health. Although general health measures, antenatal supervision, knowledge of special procedures such as immunisation against rubella and measures to prevent accidents in the home can have a profound effect on foetal and infant loss, these are not used or appreciated to the full extent by the population, and health propaganda deserves much more emphasis than it receives at present.

High standards of professional care, continued research, extension of community health programmes and education of the population in health measures can continue to improve the impressive fall in infant mortality and morbidity which has taken place during this century.

APPENDIX A

CLINICAL AND PATHOLOGICAL FINDINGS IN 103 CASES OF NEONATAL DEATH

INDEX

Case Summaries

Serial

1A

1. BIRTH TRAUMA

A. Premature Infants

Case 128

Clinical details. Male aged one day. Birth weight 2lbs 5ozs. No adverse maternal or foetal factors known. Clinical details of delivery not known (born and died in a German hospital).

Autopsy findings. Widespread intracranial haemorrhage. Incomplete rotation of large gut. Patent foremen ovale.

Histology. Primary atelectasis of the lungs.

Case 160

Clinical details. Female aged 2 days. Birth weight 3lbs 4ozs. No adverse maternal, delivery or foetal factors. Regular respiration never established. Infant showed cerebral irritation.

Autopsy findings. Intracranial haemorrhage. Two tentorial tears. Atrial septal defect.

Histology. Broncho-pneumonia changes in the lungs.

Case 207

Clinical details. Female aged one day. Birth weight 4 lbs 12 ozs. No adverse maternal, delivery or foetal factors. Irregular respirations from birth.

Autopsy findings. Widespread intracranial haemorrhage. Patent foremen ovale.

Histology. Primary atelectasis, hyaline membrane formation and early broncho-pneumonic changes in the lungs.

Case 190

Clinical details. Female aged one day. Birth weight 3lbs 9 ozs. Breech delivery, initial condition good, but rapid deterioration.

Autopsy findings. Subarachnoid haemorrhage with damage to tentorium and falx cerebri.

Histology. Primary atelectasis and incipient hyaline membrane in the lungs.

Case 185 | Clinical details. Male aged 7 days. Birth weight 3lbs 4ozs. Traumatic delivery. Showed apnoeic attacks and head retraction.

Autopsy findings. Extensive subarachnoid haemorrhage.

Histology. Lungs showed partial primary atelectasis.

Case 50 | Clinical details. Male aged 4 days. Birth weight 4lbs 2ozs. Mother suffered from hypertension and delivery effected by forceps after transverse arrest. Infant appeared satisfactory for 72 hours then developed apnoeic attacks with grey pallor. The anterior fontanelle was tense.

Autopsy findings. Widespread intracranial haemorrhage, with petechiae of pericardium.

Serial 1B | B. Non-premature infants

Case 135 | Clinical history. Female aged 7 hours. Maternal pre-eclamptic toxaemia, delivery was rapid. The infant was blue and cold from birth.

Autopsy findings. Widespread intracranial haemorrhage with petechiae of pleura, pericardium and thymus.

Case 169 | Clinical history. Male aged ½ hour, delivered by forceps. Regular respirations never established.

Autopsy findings. Intracranial haemorrhage with 2 tears in the tentorium cerebelli.

Histology. Primary pulmonary atelectasis.

Case 343 | Clinical history. Male aged 3 hours. Delivered post-mature as a breech presentation. Regular respirations never established.

Autopsy findings. Intracranial haemorrhage with torn tentorium cerebelli.

Histology. Nothing significant.

Case 219 | Clinical history. Male aged 36 hours, further details missing.
Autopsy findings. Intracranial haemorrhage with tear of tentorium and left sigmoid sinus. Patent foremen ovale. Haematoma of pericardium and tear in liver with haemoperitoneum.
Histology. Evidence of inhalation of liquor amnii and early infective features.

Case 41 | Clinical history. Male aged 3 days, delivered from an elderly primipara with hydramnios. Slow response to resuscitation, showed petechiae of lips and had a "cerebral" cry.
Autopsy findings. Intercranial haemorrhage with torn falx cerebri. Pericardial petechiae.
Histology. Nothing significant (no lung material).

Case 20 | Clinical history. Male aged 4 days. Mother suffered from diabetes mellitus, delivery was difficult with impaction of the shoulders, the infant was hypoglycaemic. Cyanosis, respiratory distress and twitching noted.
Autopsy findings. Widespread subarachnoid haemorrhage. Anomalous ribs and absence of right kidney.
Histology. Pulmonary atelectasis.

Case 233 | Clinical history. Male aged 7 days. No adverse maternal or delivery factors apparent. Developed laboured respirations and tense anterior fontanelle 24 hours after birth.
Autopsy findings. Massive intracranial haemorrhage.

2. FRANK INFECTIVE PROCESSES

A. Premature Infants

Serial 2Ai

i. Pneumonia

Case 15 | Clinical history. Female aged 2 days. Birth weight 2lbs 6ozs. Mother suffered from mitral valvular disease of the heart and

tuberculous cervical adenitis. Infant responded slowly to resuscitation, developed cyanotic attacks with hyperpyrexia and signs of consolidation of the bases of the lungs.

Autopsy findings. Pleural and pericardial petechiae. Broncho-pneumonia.

Case 10

Clinical history. Male aged 3 days. Birth weight 2lbs 12ozs. Mother was elderly and had had 3 miscarriages in the past 14 years. Infant appeared to progress for 2 days, then became grey and lethargic.

Autopsy findings. Broncho-pneumonia. Undescended testicles.

Serial 2Aii

ii. Septicaemia

Case 145

Clinical history. Male aged 10 days. Birth weight 3lbs. No adverse maternal, delivery or foetal factors recognised. Infant satisfactory for 7 days, then developed cyanosis and Cheyne-Stokes respirations.

Autopsy findings. Petechiae of pericardium and lungs. Thrombosed cerebral venous sinuses.

Histology. Myocardial and lung abscesses, containing staphylococci, organisms also present in the thrombi.

B. Non-Premature Infants

Serial 2Bi

i. Pneumonia

Case 136

Clinical history. Male aged 2 days, delivered as a face presentation. Appeared well until the second day when developed convulsions and condition deteriorated rapidly.

Autopsy findings. Haemorrhagic pneumonia, confluent in the left lung.

Histology. Haemorrhagic mononuclear pneumonia.

Case 35 | Clinical history. Female aged 3 days, born as a breech presentation. Showed continuous vomiting after each feed, became lethargic with shallow respirations.

Autopsy findings. Widespread pneumonic consolidation of the lungs.

Case 54 | Clinical history. Female aged 4 days. No adverse maternal, delivery or foetal factors known. Well for 3 days then became listless with a poor colour, developed hyperpyrexia with signs of consolidation in the lungs.

Autopsy findings. Pericardial petechiae. Widespread pneumonic consolidation of the lungs with early pleurisy.

Case 150 | Clinical history. Female aged 5 days. No adverse maternal, foetal or delivery factors recognised. Well for 4 days then developed pulmonary signs with cyanosis. A Freidlander's bacillus isolated from a throat swab.

Autopsy findings. Intense tracheitis and haemorrhagic pulmonary consolidation. Sero-sanguineous left pleural effusion.

Histology. Mononuclear and giant-cell pneumonia, necrosis of bronchial epithelium, degenerative myocarditis and haemorrhages in suprarenals.

Case 227 | Clinical history. Male aged 6 days. Mother developed influenza post-partum. Infant developed upper respiratory infection with crepitations at lung bases after 3 days. Intense physiological jaundice.

Autopsy findings. Multiple pulmonary abscesses and bilateral empyemata.

Histology. Acute suppurative pneumonia.

Case 222 | Clinical history. Female aged 8 days. No adverse maternal, delivery or foetal factors recognised. Infant well until seventh day, then developed a severe upper respiratory tract infection.

Autopsy findings. Haemorrhagic broncho-pneumonia. Intraventricular septal defect.

Histology. Widespread broncho-pneumonia.

Serial 2Bii

ii. Viral Hepatitis

Case 214 | Clinical history. Female aged 2 days. Mother was Rh negative, but infant showed a negative Direct Coombs' test. Developed deep jaundice, serum bilirubin rising to 35 mgm per 100 ml.

Autopsy findings. No kernicterus. Haemorrhage into stomach. Enlarged liver and spleen. Haemorrhages into renal pelvis, kidney and skin (petechiae).

Histology. No evidence of syphilis nor erythroblastosis. Intralobular hepatic necrosis with polymorph infiltration. Early pneumonia.

3. CONGENITAL DISEASE

Serial 3A

A. Premature Infants

Case 94 | Clinical history. Female aged 2 days. Birth weight not stated. No adverse maternal or delivery factors recognised. Infant failed to respond and showed continuous vomiting of feeds.

Autopsy findings. Almost complete pyloric stenosis. Malrotation of large gut. Pulmonary atelectasis.

Case 121 | Clinical history. Male aged 2 days. Birth weight 3lbs 8ozs. No adverse maternal or delivery factors noted. Infant born with blue asphyxia and developed cyanotic attacks after

	resuscitation.
	Autopsy findings. Abnormal pulmonary artery distribution with gross right ventricular hypertrophy.
	Histology. Nothing of note.
Case 232	Clinical history. Female aged 7 days. Birth weight 4lbs 14ozs. Mother Rh negative. Undiagnosed twin pregnancy, second twin macerated. Direct Coombs' test on first (liveborn) twin negative. Infant oedematous with bradycardia, intermittent cyanosis and grossly abnormal ECG.
	Autopsy findings. Deformed tricuspid valve with hypertrophy of the right atrium and patent foramen ovale.
Serial 3B	B. Non-Premature Infants
Case 3	Clinical history. Female aged one day. No adverse maternal or delivery factors recognised. Infant cyanosed from birth and lungs showed moist sounds.
	Autopsy findings. Coarctation of the aorta.
Case 46	Clinical findings. Female aged 5 hours. No adverse maternal or delivery factors noted. Infant showed exomphalos.
	Autopsy findings. Exomphalos continuing most of gut. Intestine plum-coloured. Transverse mesocolon torn.
Case 162	Clinical history. Male aged one hour. No adverse maternal or delivery factors noted. Infant did not establish normal respirations.
	Autopsy findings. Left dome of diaphragm absent. Left lobe of liver, stomach, spleen, small intestine and part of colon in thorax. Heart and underdeveloped lungs squeezed against right side of thorax. Left lung vestigial.

Case 195 | Clinical history. Male aged 10 hours. No adverse maternal or delivery factors noted. Infant cyanosed from birth.

Autopsy findings. Transposition of the great vessels.

Case 204 | Clinical history. Male aged one hour. No adverse maternal or delivery factors recognised. Infant had deformed ears, was born in a state of asphyxia pallida and did not respond to resuscitation.

Autopsy findings. Agenesis of kidneys.

Histology. Pulmonary atelectasis.

Case 209 | Clinical history. Female aged a few hours. No adverse maternal or delivery factors noted. Infant had a hair-lip; failed to respond to resuscitation.

Autopsy findings. Hair-lip. Coarctation of the aorta.

Case 221 | Clinical history. Female aged 2 hours. No adverse maternal or foetal factors noted. Infant had gross sympus deformity.

Autopsy findings. Sympus deformity with numerous skeletal abnormalities. Absence of rectum and renal tract.

Histology. Confirmed sex as female (ovarian tissue).

Case 74 | Clinical history. Male aged 2 days. Forceps assisted delivery. Cyanosis with apnoeic attacks from birth, systolic murmur noted.

Autopsy findings. High intraventricular septal defect with common arterial trunk.

Case 69 | Clinical history. Male aged 3 days. No adverse maternal or foetal factors noted. Infant cyanosed from birth, with bradycardia.

Autopsy findings. Virtual absence of intra-auricular septum (cor triloculare).

Case 101 — Clinical history. Male aged 5 days. No adverse maternal or delivery factors recognised. Infant cyanosed from birth with cardiomegaly and a systolic murmur.

Autopsy findings. Atrial septal defect, very narrow pulmonary artery with deformed valves.

Case 38 — Clinical history. Male aged 5 days. No adverse maternal or delivery factors noted. Infant suffered from continuous vomiting.

Autopsy findings. Atresia of lower ileum. Early peritonitis.

Case 98 — Clinical history. Female aged 5 days. No adverse maternal or delivery factors noted. Infant suffered cyanotic attacks.

Autopsy findings. Coarctation of the aorta. Intraventricular septal defect.

Case 196 — Clinical history. Female aged 9 days. No adverse maternal or delivery factors noted. Infant had cyanotic attacks, ECG showed right ventricular hypertrophy.

Autopsy findings. Transposition of the great vessels.

Case 218 — Clinical history. Male aged 10 days. No adverse maternal or delivery factors noted. Infant difficult to resuscitate after birth, ECG showed right ventricular hypertrophy. Serum bilirubin 21 mgm per 100 ml on the seventh day.

Autopsy findings. Deep jaundice. Atresia of common bile duct.

Case 7 — Clinical history. Male aged 10 days. No adverse maternal or delivery factors noted. Infant suffered from attacks of cyanosis.

Autopsy findings. Hypertrophy of left ventricle. Enlarged liver. Petechiae of cerebrum.

Histology. Marked proliferative endarteritis of small pulmonary vessels (Ayerza's disease).

4 ERYTHROBLASTOSIS FOETALIS

Serial 4 A

A. Premature Infants

Case 56

Clinical history. Male aged ½ hour. Mother was Rh negative, had previous history of blood transfusion and developed pre-eclamptic toxaemia. Infant delivered by Caesarian section. Hydropic, direct Coombs' test strongly positive.

Autopsy findings. Gross external and internal oedema. Enlarged liver, spleen and suprarenal glands. Petechial haemorrhage of suprarenals, kidney and pericardium.

Histology. Widespread erythropoetic activity in many organs. Degenerative myocarditis. Lipid deposits in suprarenal cortex. Persistence of Langhan's layer in the oedematous placenta.

Case 194

Clinical history. Female aged 8 hours. Birth weight 5lbs 4ozs. Mother Rh negative with high Anti-D antibody titre in serum. Had history of blood transfusion in infancy. During pregnancy suffered from mild toxaemia. Infant born oedematous, direct Coombs' test positive, haemoglobin 60%, serum bilirubin 4.8 mgm per 100 ml. Died during exchange transfusion.

Autopsy findings. External and internal oedema, enlarged liver and spleen.

Histology. Widespread erythropoetic activity many organs. Severe liver degeneration. Lungs showed incipient hyaline membrane formation.

Serial 4B

B. Non-Premature Infants

Case 109

Clinical history. Female aged 5 hours. Mother Rh negative with serum antibodies. Infant showed jaundice (bilirubin 14 mgm), anaemia (Hb 90%) and oedema. Direct Coombs' test positive.

Died during exchange transfusion.

Autopsy findings. Icteric. Petechiae of brain. External and internal oedema with effusions into body cavities. Enlarged liver and spleen, suprarenal cortex waxy.

Case 184 Clinical history. Male aged a few hours. Mother Rh negative with antibodies in serum. Oedematous infant born by Caesarian section. Showed jaundice (bilirubin 14 mgm), anaemia (Hb 40%) and oedema. Died during exchange transfusion.

Autopsy findings. Icteric, petechiae of brain, enlarged liver and spleen, effusions into serous cavities, pulmonary atelectasis.

Serial 5

5. TRAUMA (other than birth injury)

Case 78 Clinical history. Female aged 10 days. Full-term at birth. Killed outright in a road traffic accident.

Autopsy findings. Extensive multiple injuries.

6. NO PRECISE PATHOLOGICAL CAUSE OF DEATH

Serial 6Ai

A. Maternal, delivery or foetal factors recognised

i. Premature Infants

Case 11 Clinical history. Male aged one day. Birth weight 2 lbs 5ozs. Delivery was traumatic. Respirations slowly established, then infant developed cyanotic attacks.

Autopsy findings. Cyanosis. General congestion. Pulmonary atelectasis. Petechiae of thymus, pericardium and suprarenal glands.

Histology. Pulmonary atelectasis with hyaline membrane formation. Some mononuclear infiltration of lungs.

Case 189 Clinical history. Male aged less than one day. Birth weight 2lbs 10ozs. Labour precipitate. Infant suffered from dyspoenic attacks.

Autopsy findings. General congestion and pulmonary atelectasis.

Case 197 Clinical history. Male aged one day. Birth weight 3lbs 8ozs. Labour precipitate. Infant did not establish normal respirations, remained cyanotic.

Autopsy findings. Nothing of note beyond congestion.

Case 148 Clinical history. Male aged 2 days. Birth weight 5lbs 2ozs. Delivered by forceps after transverse arrest. Infant developed cyanotic attacks.

Autopsy findings. Cyanosis. Pulmonary atelectasis and pericardial petechiae.

Histology. Patchy pulmonary atelectasis with areas of haemorrhage and inhaled liquor amnii.

Case 29 Clinical history. Female aged one hour. Birth weight 2lbs 6ozs. Mother suffered from antepartum haemorrhage, infant delivered by breech presentation. Gasped only, respirations not established.

Autopsy findings. Congestion and pulmonary atelectasis.

Case 228 Clinical history. Male aged one hour. Birth weight not stated. Second of twins. First delivered by normal spontaneous delivery, this infant forceps assisted breech delivery. No true respiratory efforts made, only gasped.

Autopsy findings. Pulmonary atelectasis.

Case 211 Clinical history. Female aged 2 days. Birth weight 2lbs 6ozs. Mother suffered from pre-eclamptic toxaemia and antepartum haemorrhage, delivery by breech presentation, arrested. Infant very poor colour.

Autopsy findings. Little abnormal.

Histology. Pulmonary atelectasis with some polymorph infiltration.

Case 126 Clinical history. Male aged less than one day. Birth weight 3lbs 9ozs. Maternal ante-partum haemorrhage, delivery rapid, breech

presentation. Infant showed cyanosis and apnoeic attacks.

Autopsy findings. Congestion general. Pulmonary atelectasis.

Histology. Primary pulmonary atelectasis with incipient hyaline membrane formation.

Case 223 — Clinical history. Male aged one day. Birthweight 4lbs 7ozs. Maternal ante-partum haemorrhage. Infant born shocked and slow to breathe.

Autopsy findings. General congestion. Pulmonary atelectasis. Patent foremen ovale. Undescended testicles.

Case 239 — Clinical history. Male aged 2 days. Birth weight 3lbs 12 ozs. Maternal ante-partum haemorrhage, low rupture of membranes. Infant showed very slow establishment of respiration.

Autopsy findings. General congestion. Pulmonary atelectasis. Undescended testicles.

Case 133 — Clinical history. Female aged 4 hours. Birth weight 2 lbs. Membranes ruptured 4 weeks before birth. Infant suffered from cyanotic attacks.

Autopsy findings. General congestion only.

Histology. Pulmonary atelectasis with inhalation of liquor amnii.

Case 53 — Clinical history. Male aged 4 days. Birth weight 2lbs 13ozs. Mother suffered from pyelitis. At birth infant in a state of asphyxia pallida and showed spasticity.

Autopsy findings. Only congestion and cyanosis.

Case 4 — Clinical history. Male aged 2 hours. Birth weight 4 lbs 15 ozs. Infant delivered by Caesarian section undertaken because of foetal distress. Infant narcotised at birth, failed to respond.

Autopsy findings. Pulmonary atelectasis. Patent foramen ovale.

Case 147 | Clinical history. Female aged ½ hour. Birth weight 4lbs 5ozs. Mother suffered from ante-partum haemorrhage due to placenta praevia. Infant delivered by Caesarian section in a state of asphyxia pallida and only occasional breaths taken.

Autopsy findings. Little beyond petechiae of pleura and pericardium.

Histology. Primary pulmonary atelectasis with inhalation of liquor amnii.

Case 178 | Clinical history. Male aged a few hours. Birth weight 3lbs. One of twins (see Case 179). Maternal ante-partum haemorrhage with placenta praevia. Born by Caesarian section, failed to respond.

Autopsy findings. Pulmonary atelectasis.

Histology. Primary atelectasis, inhaled liquor amnii and incipient hyaline membrane formation.

Case 179 | Clinical history. Male aged 6 hours. Birth weight 2lbs 13ozs. One of twins (see Case 178). Maternal ante-partum haemorrhage with placenta praevia. Born by Caesarian section, failed to respond.

Autopsy findings. Pulmonary atelectasis.

Histology. Primary atelectasis with early hyaline membrane formation.

Case 170 | Clinical history. Female aged 12 hours. Birth weight 5lbs 4ozs. Maternal ante-partum haemorrhage and placenta praevia. Infant delivered by Caesarian section, developed cyanotic attacks.

Autopsy findings. General congestion, petechiae of pleura and pericardium. Intra-atrial septal defect.

Histology. Pulmonary atelectasis, inhalation of liquor amnii, hyaline membrane formation.

Case 21 — Clinical history. Female aged 30 hours. Birth weight 5lbs. Born by Caesarian section from mother with pre-eclamptic toxaemia. One of twins (see case 23), found dead in cot.
Autopsy findings. Little beyond petechiae of pleura and pericardium.

Case 23 — Clinical history. Female aged 4 days. Birth weight 2lbs. One of twins (see Case 21) born by Caesarian section from mother with pre-eclamptic toxaemia. Developed cyanotic attacks.
Autopsy findings. Pulmonary atelectasis.

Case 80 — Clinical history. Female aged one day. Birth weight 3lbs 9ozs. Born by Caesarian section undertaken because of maternal pelvic disproportion. Never fully developed respiration, developed cyanotic attacks.
Autopsy findings. Cyanosis, general congestion and pulmonary atelectasis.

Serial 6Aii

ii. Non-Premature Infants

Case 131 — Clinical history. Male aged one day. Post-mature, respirations poor with cyanotic attacks.
Autopsy findings. Petechiae of face and brain with general congestion.
Histology. Atelectasis with hyaline membrane formation.

Case 142 — Clinical history. Female aged 9 hours. Anaemic, direct Coombs' test negative. Developed cyanotic attacks. Haemoglobin 110%.
Autopsy findings. Pulmonary atelectasis.
Histology. Atelectasis with hyaline membrane formation.

Case 40 — Clinical history. Female aged 3 days. Born with evident ascites, well for 2 days then rapid respiratory and cardiac failure.

Autopsy findings. General congestion, petechiae pleura, patent foramen ovale. Considerable ascites present, but no cause for this found.

Histology. Pulmonary atelectasis.

Case 8 — Clinical history. Female aged 6 hours. Maternal toxaemia. Infant born face to pubis presentation. ⅓ of placenta infarcted. Infant in a state of asphyxia pallida.

Autopsy findings. Pulmonary atelectasis and pleural petechiae.

Case 165 — Clinical history. Female aged 2 days. Mother had positive Kahn test. Infant "born in a caul", meconium-stained liquor amnii. Direct Coombs' test negative. Infant responded initially then collapsed.

Autopsy findings. General congestion, pleural petechiae, liver enlarged, not fibrotic. Placenta fibrosed and calcified.

Histology. Atelectasis with inhalation of liquor amnii. No evidence of congenital syphilis.

Case 191 — Clinical history. Male aged ½ hour. Delivered by forceps for arrest. Cord round neck. Infant in a state of asphyxia pallida and did not respond.

Autopsy findings. Cyanosis, pulmonary atelectasis and pleural petechiae.

Case 24 — Clinical history. Male aged 36 hours. Mother suffered from toxaemia and hydramnics. Infant cyanosed.

Autopsy findings. Ear deformity, ostia of eyes small, partial absence of palate, small larynx, right testicle not descended. General cyanosis and pericardial petechiae.

Histology. Congestion and atelectasis.

Case 149 — Clinical history. Male aged 5 days. Mother suffered from severe pre-eclamptic toxaemia, delivery by breech presentation

with forceps assistance. Infant cyanotic and commenced vomiting after initial response.

Autopsy findings. General congestion and pulmonary atelectasis.

Histology. Atelectasis and inhalation of liquor amnii.

Case 34 — Clinical history. Female aged 8 hours. Delivered by Caesarian section because of maternal toxaemia. Infant difficult to resuscitate, showed cyanosis with shallow respirations.

Autopsy findings. Cyanosis, general congestion and pulmonary atelectasis.

Histology. Atelectasis with hyaline membrane formation.

Case 43 — Clinical history. Male aged 12 hours. Delivered by Caesarian section because of previous Caesarian section. Cord bled, infant cyanotic with 83% haemoglobin.

Autopsy findings. Cyanosis, general congestion, pulmonary atelectasis, patent foramen ovale.

Histology. Atelectasis with hyaline membrane formation.

Case 123 — Clinical history. Male aged 12 hours. Maternal toxaemia, infant delivered by Caesarian section because of foetal distress. Infant limp, initial response then died suddenly.

Autopsy findings. Cyanotic, petechiae pericardium, pulmonary atelectasis and right hydrocele.

Case 125 — Clinical history. Male aged ½ hour. Maternal toxaemia, meconium stained liquor for 36 hours, delivery by Caesarian section because of foetal distress. Infant cyanosed, meconium in respiratory tree.

Autopsy findings. General congestion, pulmonary atelectasis.

Case 192 — Clinical history. Male aged 8 hours, delivered by Caesarian section because of maternal pelvic disproportion. Infant

developed cyanotic attacks after initial response.

Autopsy findings. General congestion, pulmonary atelectasis, patent foramen ovale.

Histology. Atelectasis, inhalation liquor amnii and incipient hyaline membrane formation.

Case 73 — Clinical history. Female aged 1½ hours. Mother suffered from diabetes, toxaemia and hydramnios, infant delivered by Caesarian section. Had cyanotic attacks from birth.

Autopsy findings. General congestion and pulmonary atelectasis.

Histology. Atelectasis with hyaline membrane formation. Islets of Langerhans in pancreas grossly enlarged.

Case 230 — Clinical history. Female aged 2 days. Delivered by Caesarian section, was cyanotic from birth.

Autopsy findings. Pulmonary atelectasis.

Histology. Atelectasis with incipient hyaline membrane formation.

Serial 6Bi

B. No Maternal, Delivery or Foetal Factors Evident

i. Premature Infants

Case 2 — Clinical history. Male aged one day. Birth weight 4lbs. Intensely cyanosed at birth with intermittent gasping respirations, failed to respond.

Autopsy findings. General congestion, pulmonary atelectasis, petechiae pericardium and thymus, haemorrhage in suprarenal gland.

Case 76 — Clinical history. Male aged 2 hours. Birth weight 2 lbs. Regular respirations never established.

Autopsy findings. Cyanosed, general congestion, pulmonary atelectasis, haemorrhage in suprarenal.

Histology. Atelectasis.

Case 146 | Clinical history. Male aged 7 hours. Birth weight 3lbs 11ozs. Cyanotic from birth with grunting respiration and marked subcostal retraction.

Autopsy findings. Cyanosis and pulmonary atelectasis.

Case 157 | Clinical history. Female aged 12 hours. Birth weight 4lbs 1oz. Respirations shallow initially then irregular.

Autopsy findings. Pericardial petechiae, oedema of bronchi.

Histology. Atelectasis, inhalation of liquor amnii and incipient hyaline membrane formation.

Case 186 | Clinical history. Male aged 4 hours. Birth weight 11b 8ozs. After birth only gasped.

Autopsy findings. Congestion general, pulmonary atelectasis, ecchymosis of pleura and pencardium. Large patent foramen ovale.

Histology. Atelectasis.

Case 193 | Clinical history. Male aged a few hours. Birth weight not stated. Mother Rh negative, no antibodies. Infant showed poor respiratory efforts with rib and sternal retraction. Direct Coombs' test negative.

Autopsy findings. General congestion with petechiae of pleura, pericardium and brain. Patent foramen ovale.

Histology. Atelectasis with inhalation of liquor amnii and incipient hyaline membrane formation.

Case 62 | Clinical history. Female aged 1½ days. Cyanosed from birth.

Autopsy findings. Cyanosis and general congestion, petechiae of pericardium.

Case 172 | Clinical history. Female aged 2 days. Birth weight 5lbs 6ozs. Cyanotic attacks from birth.

Autopsy findings. General congestion and pulmonary atelectasis.

Histology. Atelectasis with hyaline membrane formation.

Case 198 — Clinical history. Male aged 1½ days. Birth weight 3lbs 4ozs. Mother Rh negative, but infant's Hb normal. Born and died in German hospital of "asphyxia".

Autopsy findings. Pulmonary atelectasis.

Histology. Atelectasis.

Case 9 — Clinical history. Male aged 3 days. Birth weight 3lbs 8ozs. Poor colour and gasping respirations.

Autopsy findings. Petechiae brain, pleura and pericardium. Pulmonary atelectasis.

Case 122 — Clinical history. Male aged 3 days. Birth weight 4lbs 1oz. Cyanotic attacks from birth.

Autopsy findings. General congestion and cyanosis. Hypospadias.

Histology. Marked pulmonary emphysema.

Case 188 — Clinical history. Male aged 3 days. Birth weight 3lbs 1oz. Mother Rh negative, but no Rh antibodies in serum. Infant had poor respiratory efforts since birth.

Autopsy findings. Pulmonary atelectasis.

Case 134 — Clinical history. Male aged 5 days. Birth weight 1lb 6½ozs. Grossly premature.

Autopsy findings. Patchy pulmonary atelectasis.

Case 176 — Clinical history. Male aged 10 days. Birth weight 2lbs 4ozs. Developed irregular respirations and cyanotic attacks.

Autopsy findings. General congestion and cyanosis. Simple cyst of liver.

Serial 6Bii

ii. Non-Premature Infants

Case 138 — Clinical history. Female aged one day, cyanotic attacks from birth.

Autopsy findings. Pulmonary atelectasis.

Histology. Atelectasis and hyaline membrane formation.

Case 173 | Clinical history. Female aged 3 hours. Mother Rh negative, no Rh antibodies in serum. Infant's respirations never fully established; direct Coombs' test negative.

Autopsy findings. Pulmonary atelectasis.

Histology. Atelectasis with inhalation of liquor amnii.

Case 112 | Clinical history. Male aged 5 days. Found dead in cot.

Autopsy findings. General congestion. Petechiae of pleura.

Case 156 | Clinical history. Female aged 9 days. Found dead in cot.

Autopsy findings. General congestion with petechiae of heart, lungs and pleura. Some vomitus in the respiratory tree.

Case 72 | Clinical history. Female aged 10 days. Found dead in cot.

Autopsy findings. Cyanosis, general congestion, petechiae of heart and lungs.

Case 175 | Clinical history. Male aged 10 days. Had some diarrhoea, turned blue when being nursed and died on mother's knee.

Autopsy findings. Deformity of right side of mouth with 2 accessory auricles on cheek. Hypospadias. General congestion.

Histology. Haemosiderin-containing macrophages in lung alveoli.

Case 55 | Clinical history. Female aged 12 days, well for 11 days then developed cyanotic attacks.

Autopsy findings. General congestion, petechiae of brain, pleura, pericardium and thymus. Marked mesenteric adenitis. Meckel's diverticulum present.

Case 235 | Clinical history. Male aged 12 days. Failed to thrive with wasting, polyuria and polydipsia.

Autopsy findings. Wasted. General congestion and pulmonary atelectasis.

Histology. Atelectasis. Adrenal cortical hyperplasia.

APPENDIX B

CLINICAL AND PATHOLOGICAL FINDINGS IN 64 CASES OF INFANTS DYING AFTER SERIOUS ILLNESS

INDEX

1. GASTRO-ENTERITIS

A. Acute

i. Uncomplicated

Serial 1Ai

Case 85 — Clinical history. Male aged 1½ months who died in July after a 3 day history of diarrhoea and vomiting of increasing severity.
Autopsy findings. Marked dehydration. Large and small intestines dilated and hyperaemic, congested gastric mucosa.
Conclusion. Dehydration and toxaemia due to gastro-enteritis.

Case 48 — Clinical history. Male aged 4 months died in December after history of intractable vomiting and diarrhoea for 5 days.
Autopsy findings. Stomach dilated, mucosa ulcerated and lumen contained altered blood. Small intestine dilated, liver appeared fatty, small pleural effusion, but no evidence of pneumonia.
Conclusion. Gastritis, aetiology undetermined.

Case 108 — Clinical history. Female aged 9 months, died in November after a few days history of acute gastro-intestinal symptoms.
Autopsy findings. Stomach and intestines dilated and congested with scattered petechiae especially in lower ileum. Slight pulmonary congestion.
Conclusion. Toxaemia from acute gastro-enteritis.

Case 158 — Clinical history. Female aged 2 months, died in December after a 2½ day history of vomiting followed by diarrhoea. Developed severe dehydration which did not yield to intensive treatment.
Autopsy findings. Dehydrated. Intestines dilated and enlarged mesenteric lymph nodes. Lungs congested.
Histology. Kidneys showed lower nephron nephrosis, intestines acute inflammatory changes.

Conclusion. Enteritis associated with lower nephron nephrosis due to dehydration.

Case 107 — Clinical history. Male aged 5 months died in November after 7 days history of diarrhoea and vomiting.

Autopsy findings. Extremely dehydrated. Congestion and haemorrhage stomach, intestines and mesentery. Acute mesenteric adenitis. Congestion elsewhere, liver showed fatty degeneration.

Conclusion. Acute gastro-enteritis.

Case 88 — Clinical history. Male aged 11 months, died in July after 24 hours history of vomiting and diarrhoea.

Autopsy findings. Congested intestine, especially terminal ileum, with hyperaemia, marked, of Peyer's patches. Basal congestion of lungs.

Conclusion. Toxaemia associated with acute gastro-enteritis.

Serial 1Aii

ii. With Concomitant Infection Elsewhere

Case 102 — Clinical history. Female aged 7 months, died in October after 2 days illness with diarrhoea, vomiting and a hoarse cough. Developed dehydration, cyanosis and râles at bases of lungs.

Autopsy findings. Dehydrated. Basal congestion of lungs. Congested intestines with acute mesenteric adenitis.

Histology. Inflammation of intestines and early pneumonia.

Conclusion. Acute gastro-enteritis, developing pneumonia.

Case 104 — Clinical history. Male aged 5 months, died in November after a history of 3 days diarrhoea and latterly vomiting.

Autopsy findings. Congested intestine, acute mesenteric adenitis, degeneration of liver and pneumonia.

Histology. Confirmed naked-eye findings.

Conclusion. Broncho-pneumonia following acute gastro-enteritis.

Case 216 | Clinical history. Female aged 4 months who died in January. Developed abscess of parotid gland and bilateral otitis media, both treated. Then developed vomiting and diarrhoea, deteriorated rapidly after 5 days.

Autopsy findings. Bilateral otitis media, congestion lung bases, intestines congested.

Conclusion. Gastro-enteritis associated with otitis media and parotitis.

Serial 1Aiii

iii. With Previous Respiratory Infection

Case 49 | Clinical history. Female aged 2 months, died in December. Had been in hospital with bronchitis, discharged, 2 days later developed diarrhoea and vomiting and died 2 days later.

Autopsy findings. Dehydrated. Intestines congested with pin-point mucosal ulcers and haemorrhage. Small pleural effusion, no evidence of consolidation of lungs.

Conclusion. Toxaemia due to acute gastro-enteritis.

Case 89 | Clinical history. Female aged $2\frac{1}{2}$ months who died in July after a history of tonsillitis, which resolved but was followed by gastro-intestinal symptoms.

Autopsy findings. Dehydrated. Lungs congested. Patent ductus arteriosus. Liver soft and pale. Stomach congested, intestines distended with thin friable walls.

Conclusion. Toxaemia from acute gastro-enteritis.

Case 64 | Clinical history. Male aged 6 months, died in March. Had a history of upper respiratory tract infection which improved with treatment, then developed severe diarrhoea and died 24 hours later.

Autopsy findings. Dehydrated. Intestines distended, liver fatty. Patent foramen ovale.

Conclusion. Dehydration following acute diarrhoea.

Serial 1Aiv

iv. Post Surgical

Case 99

Clinical history. Male aged one month, died in October. Underwent operation for circumcision, developed diarrhoea 2 days later and died, despite intensive therapy, 2 days after that.

Autopsy findings. Dehydrated. Stomach contained altered blood, intestines dilated and congested, especially in ileum, acute mesenteric adenitis. Undescended right testicle.

Histology. Inflammation of intestines, degenerative changes liver.

Conclusion. Toxaemia and dehydration from acute enteritis.

Case 92

Clinical history. Male aged 8 months, died in August. Circumcised, 5 days later developed diarrhoea and vomiting; laparotomy performed as obstruction suspected, slight blood-stained fluid in peritoneal cavity and mesenteric adenitis. Deteriorated and died 7 days after onset.

Autopsy findings. Dehydrated, congested gastric mucosa, distended intestines, fibrinous peritonitis.

Histology. Lungs showed peribronchial infiltration. Inflammation intestines and mesenteric glands.

Conclusion. Dehydration and paralytic ileus following gastro-enteritis.

Serial 1Av

v. Chronic

Case 95

Clinical history. Female aged 3½ months, died in September after a protracted history of intermitten diarrhoea and vomiting for 26 days.

Autopsy findings. Gross emaciation. Intestines, especially

ileum, caecum and ascending colon congested with blood and mucus in lumen. Mesenteric adenitis.

Conclusion. Toxaemia consequent on gastro-enteritis.

Case 224 Clinical history. Female aged 2 months, died in February. History of intermittent diarrhoea and vomiting for nearly one month.

Autopsy findings. Marasmic. Stomach and intestines dilated and haemorrhagic, slight ascitis.

Histology. Stomach showed areas of abscess formation, early broncho-pneumonia.

Conclusion. Marasmus and broncho-pneumonia due to gastro-enteritis.

Case 97 Clinical history. Male almost one month old who died in September, after a 15 day history of diarrhoea and vomiting.

Autopsy findings. Dehydrated. Stomach and intestines dilated and hyperaemic. Mesenteric adenitis. Broncho-pneumonic consolidation of lungs. Absent gall bladder and cystic duct, the common bile duct passing directly into duodenum. High ventricular septal defect and patent ductus arteriosus.

Conclusion. Broncho-pneumonia following gastro-enteritis. Contributory factor - congenital heart disease.

Case 241 Clinical history. Male aged 4 weeks, died in April. Born prematurely by Caesarian section and suffered from diarrhoea all his brief life, uncontrolled by therapy.

Autopsy findings. Emaciated. Lungs showed basal congestion. Intestines congested but little else of note.

Conclusion. Chronic enteritis, aetiology unknown.

2. PNEUMONIA

Serial 2A

A. In Infants Born Prematurely
(but dying after the neonatal period)

Case 143

Clinical history. Male aged 20 days, birth weight 5lbs 5ozs, progressed satisfactorily until 14th day when commenced to have respiratory signs with cyanosis. Died in August.

Autopsy findings. Lungs showed patchy consolidation. Pericardial petechiae. Staphylococci isolated from lungs.

Histology. Mononuclear (giant cell) pneumonia.

Conclusion. Broncho-pneumonia.

Case 245

Clinical history. Male aged 29 days, died in May. Birth weight 5lbs 6ozs, slow to resuscitate, but after minor upsets was thriving by the 25th May. Then developed pyrexia and signs of a chest infection.

Autopsy findings. Right pleural effusion, left empyema. Lower lobes of lungs consolidated with abscesses on left side. Patent foramen ovale. Staphylococci isolated from lungs.

Histology. Pneumonia with abscess formation. Renal glomeruli swollen.

Conclusion. Suppurative pneumonia.

Case 32

Clinical history. Female aged 33 days, birth weight 5lbs, healthy and thriving for first 4 weeks then developed a superficial abscess of thorax. Signs of a pulmonary infection followed and the infant died (in August) after 2 days acute illness.

Autopsy findings. Right empyema, pneumonia with abscess cavities. A staphylococcus isolated from the lungs.

Conclusion. Suppurative pneumonia.

Serial 2B	B. In Infants With No Previous Adverse History.
Case 117	Clinical history. Female aged 2 months, died in February after a 4 day history of chest infection. Autopsy findings. Sero-sanguineous pleural effusion, patchy consolidation of lungs, pallor of myocardium. Histology. Pneumonia, predominantly mononuclear. Kidneys show some hyalinised glomeruli and proliferation of Bowman's capsule. Conclusion. Extensive bilateral broncho-pneumonia.
Case 129	Clinical history. Female aged 3 months died in April. Signs of a chest infection developed 10 days before death, appeared to resolve with treatment then relapsed with serious respiratory signs 2 days before death. Otitis media noticed in terminal stages. Autopsy findings. Otitis media. Pneumonic consolidation with abscess of left lower lobe ruptured into pleura forming broncho-pleural fistula and commencing empyema. Staphylococci isolated from abscess cavity. Histology. Pneumonia (mainly giant-cell) with abscess formation. Conclusion. Pneumonia, suppurative.
Case 66	Clinical history. Male aged 4 months, died in March after 30 hour history of respiratory symptoms. Autopsy findings. Serous pleural effusions, acute inflammation respiratory tree, patchy consolidation of lungs. Cyst of kidney. Conclusion. Acute broncho-pneumonia.
Case 237	Clinical history. Female aged 17 months, died in March after 3 days of respiratory embarrassment.

Autopsy findings. Serous pleural effusions, consolidation of left lower lobe of lungs, congestion elsewhere. Marked inflammation of respiratory tree.

Conclusion. Tracheo-bronchitis and pneumonia.

Case 84 — Clinical history. Male aged 10 months, died in July after 24 hours history of pulmonary infection. Previous episodes recorded.

Autopsy findings. Petechiae of pleura and thymus. Patchy consolidation of lungs, acute inflammation of trachea.

Histology. Mononuclear pneumonia. Polymorph infiltration of liver.

Conclusion. Broncho-pneumonia.

Case 236 — Clinical history. Male aged 11 months, died in March after 7 weeks history of recurrent fever and respiratory signs.

Autopsy findings. Pleural petechiae, lungs solid, pink in colour.

Histology. Plasma cell pneumonia with pneumocystis carinii in alveoli.

Conclusion. Pneumocystis pneumonia.

Serial 2C

C. Previous History of Infection

Case 177 — Clinical history. Male aged 5 months, died in March. Admitted to hospital with measles, developed respiratory complications and died 3 days later.

Autopsy findings. Right sided empyema. Widespread consolidation.

Conclusion. Broncho-pneumonia following measles infection.

Case 70 — Clinical history. Male aged 2½ months, died in April after an illness lasting one month, acute for last week. Admitted with

acute bronchitis, then developed morbilliform rash, became cyanosed and died suddenly.

Autopsy findings. Bilateral serous pleural effusions, congested respiratory tree, upper lobes of lungs consolidated.

Histology. Broncho-pneumonia.

Conclusion. Pneumonia sequel to measles.

Case 113 | Clinical history. Male aged 7 months, died in January after 24 hours acute respiratory symptoms, following signs of a mild upper respiratory tract infection for several days. The infant had just been discharged from hospital before this episode, having been treated for infantile eczema.

Autopsy findings. Skin showed healing eczema. Respiratory tree inflamed with many areas of haemorrhagic consolidation of the lungs. Staphylococci isolated.

Histology. Haemorrhagic pneumonia with masses of organisms morphologically staphylococci.

Conclusion. Staphylococcal pneumonia.

Case 168 | Clinical history. Male aged 19 months, died in March after an illness lasting one month, the last 6 days being acute. This infant suffered from measles, otitis media and then chickenpox, developed signs of pneumonia and died suddenly.

Autopsy findings. Petechiae of brain. Widespread pneumonic consolidation of lungs. Intra-atrial septal defect.

Histology. Acute broncho-pneumonia with areas of abscess formation.

Conclusion. Suppurative pneumonia following measles and chickenpox.

Case 110 | Clinical history. Female aged 16 months, died in December after one day's acute history of respiratory embarrassment.

Previously had suffered from mild diarrhoea.

Autopsy findings. Marked inflammation of respiratory tree, lungs showed marked congestion. Intestines congested, agonal intussusception in ileum. Mesenteric adenitis. Beta-haemolytic streptococci and staphylococcus aureus isolated from bronchial swabs.

Histology. Broncho-pneumonia with haemorrhage and hyaline membrane formation.

Conclusion. Broncho-pneumonia following mild enteritis.

Serial 2D

D. Associated with Congenital Abnormalities

Case 6

Clinical history. Female aged 7 months, died in February. Had attacks of weakness and pallor, investigations showed congenital heart disease with right ventricular hypertrophy. After one episode of broncho-pneumonia a month previously, re-admitted with relapse and died one day after commencement of this second attack.

Autopsy findings. Inflammation of respiratory tree, bilateral pneumonic consolidation. Marked hypertrophy of right ventricle but valves and great vessels normal. Petechiae of pleura and pericardium.

Histology. Pneumonia.

Conclusion. Lobar pneumonia in infant with cardiopathy of unknown aetiology.

Case 71

Clinical history. Male aged 5 weeks, died in April. Developed respiratory signs and died one week later after 24 hours acute exacerbation.

Autopsy findings. Petechiae pleurae, broncho-pneumonic consolidation of lungs, inflammation respiratory tree. Hypertrophy of heart and patent ductus arteriosus.

Conclusion. Acute broncho-pneumonia in case of congenital heart disease.

Case 124 Clinical history. Male aged 7 months, died in March. Infant was a mongol, developed an upper respiratory tract infection and died 2 days later.

Autopsy findings. Mongol. Acute inflammation respiratory tree, haemorrhagic pneumonic consolidation.

Conclusion. Broncho-pneumonia in a mongoloid infant.

Case 231 Clinical history. Male aged 3 months, died in March. After one episode of respiratory embarrassment, re-admitted with similar condition, rapid deterioration and died 2 days later.

Autopsy findings. Right pleural effusion, bilateral broncho-pneumonia. An even surfaced tumour was seen on the left vocal cord.

Histology. Broncho-pneumonia. The tumour is in the nature of a hamartoma.

Conclusion. Acute broncho-pneumonia associated with obstruction of the larynx due to a hamartoma.

3. OTHER INFECTIVE CONDITIONS

Serial 3A

A. Septicaemia

Case 163 Clinical history. Female aged 16 days, died in February. Mother suffered from hepatitis in seventh month of pregnancy. Infant developed jaundice, enlarged liver and bradycardia.

Autopsy findings. Deep jaundice. Umbilicus not infected.

Ecchymosis of pleura and peritoneum. Empyema. Abscesses of liver.

Histology. Suppurative cholangitis, bacterial clumps in adrenals, abscess in myocardium, broncho-pneumonia with commencing abscess formation, suppurative pleurisy, abscesses in kidney. Perisplenitis. Gram stain showed organisms morphologically resembling staphylococci in these sites.

Conclusion. Staphylococcal pyaemia.

Case 154

Clinical history. Male aged 5 months, died in October after 3 days history of mild diarrhoea and vomiting, then onset of cyanosis and collapse one day before death. Clinically meningococcal septicaemia suspected.

Autopsy findings. Gross congestion and oedema of brain, inflammation respiratory tree, basal congestion of lungs, petechiae of gastric mucosa. A Friedlander's bacillus was isolated from the heart blood and bronchial swabs.

Histology. Congestion and oedema of meninges with cellular infiltrate. Congestion and oedema of brain substance. Interstitial pneumonia. Degenerative changes liver and kidneys.

Conclusion. Septicaemia due to Friedlander's bacillus with acute pneumonia and early meningeal infection.

Case 13

Clinical history. Male aged 7 months, died suddenly in March after 19 hours history of purpura and chest signs.

Autopsy findings. Diffuse purpuris rash of skin. Petechiae in mesentery. Haemorrhages suprarenal glands. Patchy consolidation of lungs.

Histology. Confirmatory.

Conclusion. No organisms isolated, picture that of a fulminant meningococcal septicaemia: Freidrich - Waterhouse syndrome.

B. Of Central Nervous System

Serial 3Bi

i. Meningitis

Case 119

Clinical history. Male aged 18 months, died in February after one day's illness with signs of meningitis.

Autopsy findings. Purulent meningitis, congestion of respiratory tree.

Histology. Acute meningitis, mononuclear pneumonia with incipient hyaline membrane formation, early nephritis changes in kidneys.

Conclusion. Acute meningitis.

Case 25

Clinical history. Female aged 12 months, died in July. Infant commenced vomiting, developed an ill defined rash, conjunctivitis and deteriorated rapidly, dying one day after onset of symptoms.

Autopsy findings. Skin petechiae. Meningitis (Neisseria meningitidis isolated from base of brain and from blood). Brain showed petechiae, as did pleurae. Basal congestion of lungs. Haemorrhage adrenals.

Histology. Meningitis, interstitial pneumonia.

Conclusion. This was coded as Meningococcal meningitis, but there are features of a septicaemia.

Case 208

Clinical history. Male aged 2 months, died in December after less than twenty four hours symptoms terminating in coma. Neisseria meningitidis isolated from cerebro-spinal fluid.

Autopsy findings. Meningitis.

Histology. Confirmatory.

Conclusion. Meningococcal meningitis.

Serial 3Bii

ii. Encephalitis

Case 111

Clinical history. Male aged 6 months, died suddenly in December after an illness of ten days duration. Initially there was diarrhoea and vomiting, which resolved, but infant then became very ill, lapsed into coma and died within 24 hours of the onset of acute symptoms.

Autopsy findings. Brain considerably congested with petechiae of white matter, haemorrhage into cerebellum, congested choroid plexuses with blood in lateral ventricles. Lungs showed patchy consolidation.

Conclusion. Encephalitis with cerebellar haemorrhage.

Case 87

Clinical history. Male aged 2 months, died suddenly in July after a 7 day illness characterised by listlessness, some vomiting and terminal hyperpyrexia.

Autopsy findings. Brain congested with oedema of meninges, ante-mortem clot in posterior part of longitudenal sinus.

Histology. Confirmed clot ante-mortem. Suggestion of perivascular cuffing in brain, but no neuronophagia.

Conclusion. Cause of death longitudinal sinus thrombosis, aetiology of this, however, obscure.

Serial 3C

C. Hepatitis

Case 93

Clinical history. Male aged 3 months who died in September. Treated in a German hospital and clinical details lacking, but had been ill for 6 weeks.

Autopsy findings. Cirrhotic liver, ascites, pitting oedema lower limbs, general emaciation.

Histology. Destruction of normal hepatic architecture with nodular regeneration and portal fibrosis.

Conclusion. Cirrhosis following neonatal hepatitis.

Serial 3D

D. Peritonitis

Case 45

Clinical history. Male aged 10 months, died in October after a 3 weeks history of abdominal distension, vomiting and pyrexia following third degree burns of the wrist. Urinary infection discovered. Infant slowly deteriorated.

Autopsy findings. Small bilateral pleural effusions. Turbid peritoneal fluid, fibrinous exudate peritoneum, some inflammation intestines, liver haemorrhagic, hepatic vein thrombosed.

Conclusion. Urinary infection, peritonitis of undetermined aetiology and hepatic vein thrombosis.

Serial 4A

4. CONGENITAL ABNORMALITIES

A. Cardiac

Case 151

Clinical history. Male aged 3 weeks, developed dyspnoea then flaccid paralysis and died 2 days after onset of symptoms.

Autopsy findings. Microcephaly. Talipes. Cysts of kidneys. Pericardial effusion. Coarctation of aorta with widely patent ductus arteriosus.

Histology. Confirmed renal condition.

Conclusion. Coarctation of aorta (with polycystic disease of the kidneys).

Case 240

Clinical history. Female aged 18 days. Cardiac bruit noted at neonatal examination. Developed cyanotic attacks, large heart noted on X-ray, became apnoeic and died.

Autopsy findings. Enlarged, hypertrophied heart with a single large arterial trunk, single auricle and large ventricular septal defect, the whole constituting virtually a cor biloculare.

Conclusion. Severe congenital cardiac defect (cor biloculare).

Case 187

Clinical history. Male aged 5 weeks, congenital cardiac defect noted after birth, gradually deteriorated.

Autopsy findings. Pericardial petechiae. Heart grossly enlarged with left ventricular hypertrophy. High intraventricular septal defect, transposition of the great vessels, patent ductus arteriosus. Lungs showed patchy collapse.

Conclusion. Transposition of great vessels.

Case 130

Clinical history. Male aged 2 months. Noted to be blue in colour from birth, developed dyspnoea 5 days before death and gradually deteriorated.

Autopsy findings. Cyanosed. Enlargement of both ventricles of heart with obliteration of the right ventricular cavity by fibromuscular hyperplasia, with obliteration of pulmonary and tricuspid valves. Patent foramen ovale and ductus arteriosus, the left side of the heart dealing with both pulmonary and systemic circulation.

Conclusion. Left ventricular failure, congenital heart disease.

Case 247

Clinical history. Male aged 2 months, cyanosed from birth and for next 2 months life ran a stormy course punctuated by episodes of pneumonia.

Autopsy findings. Lungs very congested and oedematous. Cardiac enlargement, mainly of right side. Great vessels transposed, patent ductus arteriosus. Right renal vein thrombosed and right kidney disorganised with pale and plum coloured areas.

Histology. Confirmatory.

Conclusion. Transposition of great vessels.

Case 181 | Clinical history. Male aged 4 months, history of pulmonary infections, developed cyanotic attacks with syncope, died in an apnoeic attack.

Autopsy findings. Cerebral petechiae. Lungs showed alternating atelectasis and emphysema. Pericardial petechiae. Gross atrio-ventricular septal defect with abnormal distribution of pulmonary vessels.

Conclusion. Septum primum defect of heart.

Case 141 | Clinical history. Male aged 7 months, cyanosed from birth, developed syncopal attacks. Fingers clubbed, cardiac bruits.

Autopsy findings. Large aorta arising from right ventricle, small pulmonary artery with obliteration of pulmonary orifice, patent ductus arteriosus, defect intraventricular septum and patent foramen ovale, so much so that 2 separate auricles could hardly be said to exist.

Conclusion. Fallot's tetralogy.

Case 201 | Clinical history. Male aged 17 months. Recognised case of transposition of the great vessels. Developed an upper respiratory tract infection, deteriorated and died with the clinical impression of subacute bacterial endocarditis.

Autopsy findings. Deep cyanosis, oedema of legs, petechiae limbs and mesentery, inflammation upper respiratory tract, lungs congested. Marked cardiac enlargement, especially of right side. Dextro-position of aorta with stenosis, pulmonary artery arising from both ventricles with ventricular septal defect, small patent foramen ovale and large patent ductus arteriosus. Heart valves scarred and adherent, but no inflammation.

Histology. Early bronch-pneumonia, no evidence subacute endocarditis of valve cusps.

Conclusion. Fallot's tetralogy.

Case 234

Clinical history. Female aged 14 months, suffered from repeated attacks of upper respiratory infection. Terminal bronchiolitis with sudden death.

Autopsy findings. Pleural effusion. Gross cardiac enlargement, endocardium below aortic valve thick and opaque, myocardium fibriotic. Left coronary artery rose from pulmonary artery. Coarctation of aorta.

Histology. Myocardial and endocardial fibrosis. Broncho-pneumonia, reactive changes in spleen.

Conclusion. Coarctation of aorta, fibro-elastosis of heart due to anomalous coronary artery. Broncho-pneumonia.

Serial 4B

B. OF CENTRAL NERVOUS SYSTEM

Case 96

Clinical history. Female aged 6 weeks, noticed to be hydrocephalic at birth, with spina bifida. Condition steadily deteriorated.

Autopsy findings. Emaciated, skull bones widely separated. Large internal hydrocephalus with flattening of convolutions, medulla compressed into foramen magnum. Gap in posterior bodies of lumbar 1 - sacral 1 vertebrae with meningocele.

Conclusion. Hydrocephalus, Arnold-Chiari malformation. Meningocele.

Case 36

Clinical history. Female aged 2 months, had large inoperable meningocele, gradually deteriorated with paralysis and emaciation.

Autopsy findings. As in case 96.

Conclusion. Hydrocephalus and meningocele.

Case 200 | Clinical history. Female aged 3 months, born with hydrocephalus and spina bifida. Developed signs of meningitis 3 weeks before death.

Autopsy findings. Petechiae pericardium, patent foramen ovale. CNS findings as in Case 96 above, with addition of presence of pus throughout.

Histology. Widespread meningitis.

Conclusion. Hydrocephalus and meningomyelocele with unresolved meningitis.

Case 28 | Clinical history. Male aged 2 months, born with hydrocephalus and spina bifida, signs of meningitis developed.

Autopsy findings. Very similar to Case 200 above.

Conclusion. Hydrocephalus, meningomyelocele and meningitis.

Case 90 | Clinical history. Male aged 15 months developed vomiting, neck stiffness, cyanotic attacks and died after a 4 day history.

Autopsy findings. Large internal hydrocephalus with cerebral atrophy. No evidence of infection.

Conclusion. Internal hydrocephalus.

Serial 4C

C. Intestinal

Case 217 | Clinical history. Male aged one month, suffered from projectile vomiting for 14 days. Operation for pylorie stenosis performed, died 5 days later.

Autopsy findings. Poorly nourished, small pleural and pericardial effusions, right subphrenic abscess, haemorrhage in region of pylorus.

Conclusion. Congenital pyloric stenosis (post-operative death from subphrenic abscess and secondary haemorrhage).

Serial 4D

D. Hepatic

Case 137 | Clinical history. Male aged 2 months, mongoloid, cyanotic attacks

for some days after birth, then developed jaundice and gradually deteriorated.

Autopsy findings. Deeply jaundiced mongol. Ascites (bile-stained) Bile ducts not visible in cut surface of liver, gall bladder contained colourless mucoid fluid.

Conclusion. Atresia of bile ducts.

Serial 5

5 ACCIDENTAL DEATHS

Case 27

Clinical history. Female aged 19 months involved in road traffic accident, died twelve hours later.

Autopsy findings. Widespread fractures of skull.

Case 144

Clinical history. Male aged 17 months swallowed 75-100 aspirin tablets, admitted to hospital, lapsed into coma and despite treatment died some 12 hours later.

Autopsy findings. Marked cerebral oedema, congestion elsewhere. Urine gave strongly positive test for salicylates.

Conclusion. Aspirin poisoning.

APPENDIX C

CLINICAL AND PATHOLOGICAL FINDINGS IN 83 CASES OF SUDDEN OR UNEXPECTED DEATH IN INFANCY

INDEX

1. INFANTS IN WHOM AUTOPSY SHOWED SIGNS OF ASPHYXIA ONLY

(Apart from minor non-contributory, incidental findings)

Serial 1A

A. Those with no Previous Symptoms

Case 250

Clinical details. Male aged 25 days. Premature (birth weight 3lbs 10ozs), had a few pustules in the skin in early days of life which cleared up and then appeared to be thriving satisfactorily. Found dead in cot, in hospital, at 0845 hours, 1 July 1960.

Autopsy findings. General congestion of all organs. Petechiae of pleural and pericardial surfaces. Lungs expanded, congested, no consolidation detected.

Opinion. Death from asphyxia.

Histological examination. The lungs showed desquamation of the epithelium in many bronchi, the lumen containing the shed cells and the bronchi showing an empty lumen with denudation of their epithelium. Much of the lung tissue was consolidated (Fig 1) and in areas the alveoli were full of oedema fluid which showed some peripheral condensation suggestive of an early hyaline membrane (Fig 2). There was a diffuse infiltration of neutrophils, lymphocytes and large mononuclear cells into the alveolar walls, the latter often being present in the alveolar spaces, sometimes forming giant cells. The remaining organs showed congestive changes only.

Conclusion. Interstitial and mononuclear pneumonia.

Case 79

Clinical details. Female aged 8 weeks. Previously well, given a bottle at 0430 hours, 11 June 1957, the head being placed on the side. Seen by father, apparently asleep and not disturbed, at 0730, found dead by mother at 0950 hours.

Autopsy findings. Cyanosis of extremities and lips, petechial

haemorrhages on pleural and pericardial surfaces. Lungs congested, otherwise appeared normal. Remaining organs congested only.

Opinion. Asphyxia.

Histological examination. Not available.

Case 106

Clinical details. Male aged 2 months. Seen by mother at 0200 hours, 3 November 1957, asleep in carriage. Found dead at 1000 hours.

Autopsy findings. Cyanosis. Petechiae pleura and pericardium. Lungs appeared normal apart from congestion. Petechiae of thymus. Meninges and lymph nodes of neck congested.

Opinion. Asphyxia.

Histological examination. The lungs showed marked congestion with acute emphysematous changes in areas. The bronchi showed desquamation of their epithelial cells which in some cases were almost disrupted and associated with haemorrhage (Fig 3). The alveolar walls showed considerable thickening by congestion and the infiltration of large and small mononuclear cells and some polymorphs, the alveolar spaces contained similar cells, predominantly mononuclears, and haemorrhage (Figs 4 and 5). The other organs showed congestion, with areas of haemorrhage in addition in the thymus gland.

Conclusion. Interstitial and mononuclear pneumonia.

Case 31

Clinical details. Male aged 3 months. Previously well, found dead in bed 7 August 1956.

Autopsy findings. Cyanosis. General congestion, including in lungs, but no other findings of note.

Opinion. Asphyxia.

Histology. Not available.

Case 205 Clinical details. Male aged 3 months. Well the previous evening, found dead in pram, lying on his back, by the mother at 0915 hours, 8 November 1959.

Autopsy findings. Cyanosis of extremities. Petechiae of brain, intestine, endocrine glands, pleurae and pericardium. General congestion of all organs including lungs. The respiratory tree contained thin yellowish fluid and the lower lobes of the lungs were firm.

Opinion. Asphyxia.

Histological examination. The lungs showed widespread congestion and in the main appeared solid due to alternating areas of collapse and exudation (Fig 6). The bronchi showed desquamation of the epithelial cells (Fig 7) with scattered small round cells and polymorphs. There were numerous polymorphs in the alveolar walls and some small vessels showed thrombosis. The remaining organs showed congestive changes only, except that small foci of polymorphs were seen in the liver (Fig 8).

Conclusion. Acute tracheo-bronchitis and early broncho-pneumonia. Liver changes may indicate a septicaemic condition.

Case 152 Clinical details. Male aged 8 months. No history of illness. Seen apparently well, at 0300 hours, found dead in cot, face down on soft pillow, at 0630 hours, 14 October 1958.

Autopsy findings. Subconjunctival haemorrhage on right side. Petechiae of thymus, pleurae and pericardium. Larynx congested, a little frothy mucus in upper respiratory tree. Lungs heavier than normal, remaining organs congested.

Opinion. Asphyxia. ?fulminant respiratory infection.

Histological examination. The lungs showed areas of acute emphysema and general congestion. The alveolar walls were thickened in areas with large mononuclear cells in the walls and spaces (Fig 9). Remaining organs showed congestion only.

Opinion. Interstitial mononuclear pneumonia.

Case 180

Clinical details. Male aged 2½ months. Well on 14 January 1959, found dead in bed at 0730. The bed was broken with the head end down, and there was some bruising on the top of the infant's head.

Autopsy findings. No cerebral injury. Petechiae of pleurae and peritoneum. A little pink frothy material in respiratory tree. Lungs congested and oedematous. General congestion elsewhere.

Opinion. Asphyxia. As there was no evidence of cerebral damage it was considered that the broken bed was coincidental and that trauma was not responsible for death.

Histology. Not available.

Serial 1B

B. Those with Previous Mild Symptoms

Case 75

Clinical details. Male aged one month. Recent upper respiratory tract infection, not considered serious by mother. Found dead in crib, cyanosed and mottled, at 0730 hours, 27 May 1957.

Autopsy findings. Marked cyanosis. Petechiae thymus, pleura and pericardium. Upper respiratory tree congested, a few milk particles, but no obstruction. Lungs congested. Other organs congested.

Opinion. Asphyxia.

Histological examination. The lungs showed general congestion with areas of consolidation and acute emphysema. The bronchi showed areas of desquamation of their epithelium (Fig 10),

the alveolar walls were thickened with an infiltration of small mononuclear cells with a few polymorphs and large mononuclear cells, sometimes of a giant variety, were seen in the alveolar spaces (Figs 11 and 12). Remaining organs showed congestion only.

Conclusion. Interstitial and mononuclear pneumonia.

Case 251

Clinical details. Female aged 5 weeks. Off food and "niggly" for a day or two, with some diarrhoea and vomiting two days before death. Infant awoke during the night, was fed and left lying face downwards in its pram at 0330 hours (no pillow was used). Found dead by father at 0745 hours, 2 June 1960.

Autopsy findings. Cyanosis of extremities. Petechiae of the pleurae, pericardium and thymus. Lungs congested with scattered petechial haemorrhages in the substance and a little frothy mucus in the upper respiratory tree. Remaining organs congested.

Opinion. Asphyxia.

Histological examination. The lungs showed general congestion with some interstitial haemorrhages. The bronchi showed epithelial desquamation, the cells being desquamated singly rather than in blocks (Fig 13), the alveolar walls were considerably thickened and infiltrated with large and small mononuclear cells and polymorphs, the former being also seen in the alveolar spaces (Fig 14). The remaining organs were congested, the liver showed vacuolisation of the cells with some cellular pleomorphism. The kidney showed areas of necrosis and an infiltration with polymorphs (Fig 15). The myocardium showed areas of fibrosis (Fig 16).

Conclusion. Pneumonia, predominantly interstitial, with early

renal infection and myocardial fibrosis (no cardiac abnormality was found otherwise).

Case 68

Clinical details. Female aged 3 months. Born prematurely but discharged from hospital 24 February 1947, thriving. Vomited after feed at 0100 hours, 29 March and found dead by mother at 0930 hours.

Autopsy findings. Well nourished. Cyanosed finger nails. Depressed anterior fontanella. Petechiae of pericardium, pleurae and kidneys. A little frothy mucus in respiratory tree. Lungs congested and oedematous, no consolidation detected. Liver pale and fatty.

Opinion. Asphyxia, cause unknown.

Histology. None available.

Case 91

Clinical details. Male aged 2 months. Fractious during night of 17/18 August and was given a little syrup of Chloral. A few hours later found dead, face down in contact with bedclothes.

Autopsy findings. Well cared for. A little frothy sanguineous fluid in nostrils. Petechiae pericardium and pleurae. Frothy blood stained fluid in respiratory tree but no obstruction. Lungs congested, as were other organs.

Opinion. Asphyxia.

Histological examination. (No slides now remain for photography) The lungs showed extreme congestion with areas of haemorrhage and oedema. The alveolar spaces contained very numerous mononuclear cells so that sections appeared almost solid. The bronchioles were empty.

Conclusion. Mononuclear pneumonia.

Case 30

Clinical details. Female aged 3 months. This infant was "fussy" and could not sleep one evening and was seen at 2030 hours, 4 August 1956, by a medical officer who found a temperature of 100°F but nothing else abnormal on physical examination. The father was told to report to the clinic the next morning if the child was not better. He did not do so, but during the next night the infant was again "fussy", it was brought into its parents' bed and found dead at 0700 hours, 6 August.

Autopsy findings. Normal development. Cyanosis of face and neck. Some petechiae of brain, heart, thymus and pleurae. Pink, frothy material in respiratory tree. Lungs dark, congested, oedematous. Remaining organs congested.

Opinion. Asphyxia.

Histological examination. The lungs showed marked congestion with areas of oedema. The epithelium of the bronchi was desquamated (Fig 17), the alveolar walls were thick and infiltrated with large and small mononuclear cells; these were seen in the alveolar spaces where peripheral condensation of exudate showed an appearance like incipient hyaline membrane formation (Fig 18).

Conclusion. Mononuclear pneumonia predominantly interstitial.

Case 42

Clinical details. Male aged 4 months. Under the care of a medical officer for 2 days with sore throat and off his feeds; treated as a simple case of upper respiratory tract infection. Appeared to be breathing normally when parents went to bed on the night of 17/18 October, but infant found dead, under the bedclothes, at 0705 hours the next morning.

There was some dried blood around the nostrils but no evidence of external injury.

Autopsy findings. Well developed and well nourished infant with marked cyanosis of extremities. The meningeal vessels were congested and there were areas of diffuse subarachnoid haemorrhage. The tonsils were enlarged, one containing a small abscess. The upper respiratory tree was congested and contained a little mucoid and frothy blood-stained fluid. There were petechiae of the heart, thymus and ascending aorta. The lungs and other organs were congested.

Opinion. Asphyxia.

Histology. None available.

Case 81

Clinical details. Male aged 4 months. Had a recent history of possible whooping cough. Found dead in cot, lying on its face, early on the morning of 16 June 1957.

Autopsy findings. Cyanosed, well developed infant. Anterior fontanelle widely patent. There was a little frothy mucus in the main bronchi and petechiae of the pleurae. The lungs and remaining organs, especially the brain, were congested though the liver was pale.

Opinion. Asphyxia, cause unknown.

Histology. None available.

Case 174

Clinical details. Male aged four and a half months. Slight diarrhoea and vomiting for a day or two, seen by medical officer on 30 April; nothing abnormal was found on physical examination, the temperature was 98.4°F, advice was given. Seen again that evening, temperature 99.8°F, still some vomiting but nothing abnormal found and no disquiet felt. Found dead next morning, some vomitus on pillow.

Autopsy findings. Some dehydration. Upper respiratory tree contained mucus and particles of food, but there was no obstruction. The lower part of the respiratory tree contained a little mucus only. The lungs were congested and firm, the intestinal tract and remaining organs also showed congestion.

Opinion. Asphyxia. Some dehydration.

Histological examination. The lungs showed acute congestion with some emphysema, the bronchial walls showed desquamation of the epithelium and some bacterial clumps (Fig 19). The alveoli often contained oedema fluid with mononuclear cells (Fig 20). Other organs appeared healthy, although congested, except the kidney which showed swelling of the glomerular tufts and of the tubules (Fig 21).

Conclusion. Mononuclear pneumonia.

Case 26

Clinical details. Female aged 6 months. Had upper respiratory tract infection and vomiting for 3 days, treated by medical officer and appeared to respond, on the day of death it appeared well and was playing normally. The mother saw it on the evening of 19 June 1956, sleeping on its front (which was customary) and half an hour later found it dead, in the same position, with some vomitus round the mouth.

Autopsy findings. Deep cyanosis of finger and toe nails. Right otitis media with intact ear drum. The trachea was congested, but empty, the bronchi contained frothy slightly blood-stained fluid. There were numerous petechiae in the pleurae and a lesser number over the pericardium and thymus. The lungs were congested and oedematous.

Opinion. Asphyxia.

Histology. None available.

Case 199

Clinical details. Male aged 6 months. Had measles one week before death. Well when put to bed one evening, the mother heard the infant crying early next morning, took it into the parents' bed where it was found dead when the parents woke on the 25 October 1959.

Autopsy findings. Well nourished and well developed. Anterior fontanelle patent. The respiratory tree was congested, the oesophagus contained vomitus but only a few specks of this were seen in the trachea. The respiratory tract was congested, with a few petechiae over the pleural and pericardium. The lungs were congested and oedematous, elsewhere only congestive features were seen.

Opinion. Asphyxia.

Histological examination. Most of the tracheal epithelium had been desquamated, leaving a haemorrhagic almost necrotic submucosa which in areas contained small round cells and nuclear debris (Fig 22). The lungs showed general congestion with some acute emphysema. The small bronchi showed desquamation of their lining epithelium, the shed epithelium being sometimes admixed with mononuclear cells, sometimes with polymorphs as well (Fig 23). The alveoli showed thickened walls and mononuclear cells in the spaces (Fig 24). A section stained by Gram's method showed numerous gram positive cocci in clumps, chains and sometimes in diplococcal form. The remaining organs showed congestion, with marked hyperplasia of the follicles of the spleen (Fig 25) (indicating an infective process); the liver showed scattered polymorphs and the suprarenal small haemorrhages.

Conclusion. An acute tracheo-bronchitis with early mononuclear pneumonia.

Serial 1C

Case 86

C. A case Dying in the Presence of an Adult

Clinical details. Female aged 4 months. The mother had fed her infant, then went into the garden to bring her other three children. On her return, she found the infant choking. Neighbours gave artificial respiration, but on arrival at hospital the infant was found to be dead.

Autopsy findings. Diffuse cyanosis. The trachea contained semi-solid material like the stomach contents, but this was not seen, except for a few specks, further down the respiratory tree. The pleurae showed ecchymosis and the lungs and other organs were congested. The thymus was large (weighing 32g).

Opinion. Asphyxia. The degree of inhalation of stomach contents was not considered sufficient to cause obstruction and hence this case is included in the "asphyxial picture only" group although there is some overlap with the "asphyxia with inhalation of vomitus" group.

Histology. Not available.

Serial 1D

Case 226

D. A case with a Brief Acute History

Clinical details. Female aged 2 months. Infant developed normally, had a slight head cold for a few days. At 0100 on 23 February it was crying, then went to sleep. The mother noticed the child was gasping at 6 am, it continued to have laboured respirations for over an hour but was pronounced dead by a medical officer at 0730 hours. (The mother had lost another child under similar circumstances just over 2 years previously, the infant dying unexpectedly at the age of 7 months).

Autopsy findings. Well nourished infant. Small reducible umbilical hernia. There were petechiae of the pleurae, pericardium and thymus. The respiratory tree contained a little frothy material, the lungs were congested as were the other organs.

Opinion. Asphyxia.

Histological examination. The lungs showed general congestion with some emphysema. The alveolar walls were thickened with an infiltration of large and small mononuclear cells and the former were also seen lying in exudate in some alveoli (Figs 26 and 27). Remnants of haemopoesis were seen in the liver.

Conclusion. Acute interstitial pneumonia.

2. INFANTS IN WHOM AUTOPSY SHOWED EVIDENCE OF ASPHYXIA ACCOMPANIED BY THE PRESENCE OF CONSIDERABLE QUANTITIES OF INHALED VOMITUS IN THE RESPIRATORY TREE

A. Those Cases with no Previous Symptoms

Serial 2A

Case 51

Clinical details. Male aged 2 months. Found dead in his pram on the evening of 9 December 1956, cyanosed with vomitus in the mouth and nose.

Autopsy findings. Normally developed. Cyanosis of extremities. Vomitus trickling from nose and mouth on handling. General congestion of all organs. Larynx and trachea contained mucus and a large quantity of white flaky vomitus. The bronchi were full of the same material. There were petechiae of the pleurae, pericardium and thymus. The lungs were congested and a frothy blood stained fluid flowed from the cut surface. The stomach was full of undigested milk.

Opinion. Asphyxia following inhalation of food.

Histology. No material available.

Case 100

Clinical details. Male aged 2 months. Born prematurely (birth weight 5lbs), but seemed to thrive and had no symptoms or signs of illness. He was fed at 1600 hours and found dead at 2055 hours, 8 October 1957.

Autopsy findings. Well nourished and cared for, weight 7lbs 3ozs. Lips and forehead cyanosed and white milky fluid came from the mouth and nose on handling. There were marked petechiae over the pleurae and pericardium. The oesophagus, pharynx, trachea and bronchi were full of thick milky fluid. The walls of the respiratory tree were congested, as were the lungs and other organs, particularly the brain. The stomach was dilated with gas, but contained only a small quantity of milk.

Opinion. Asphyxia, inhalation of vomitus.

Histology. None available.

Case 18

Clinical details. Male aged 3 months. The infant had thrived. It was fed (from a bottle) at 0445 and found dead at 0900 hours, 6 May 1956, by an aunt. There was vomitus on the pram pillow.

Autopsy findings. Well nourished and cared for. Cyanosis of extremities. Petechiae of the pleurae, pericardium and thymus. The oesophagus, larynx, trachea and main bronchi especially the right were full of vomitus. The lungs and other organs were congested.

Opinion. Asphyxia from inhalation of vomitus.

Histology. None available.

Case 155

Clinical details. Male aged 3 months. Put to bed in a carricot at 2300 hours, had been apparently well. Heard to cry during the night, but not actually looked at by the parents until the mother found him dead at 0830 hours, 10 November 1958.

Autopsy findings. Petechiae of pleurae and spleen. The trachea and main bronchi were full of thick creamy fluid like that filling the stomach. The lungs were congested with areas of collapse.

Opinion. Asphyxia from inhaled vomitus.

Histological examination. The lungs were intensely congested, subpleural haemorrhages. The small bronchi showed desquamation of their lining epithelium and a marked peribronchial infiltration with small and large mononuclear cells (Fig 28). In areas the alveoli contained exudate with large and small mononuclear cells in the lumen (Figs 29 and 30). A section stained by Gram's method showed scattered gram positive diplococci and cocci in short chains morphologically resembling a streptococcus pneumoniae. Other organs showed congestion and in addition the kidney showed swelling of glomerular tufts and proximal tubules (Fig 31).

Conclusion. There is histological evidence of bronchiolitis and early mononuclear pneumonia.

Case 139

Clinical details. Female aged 4 months. The mother was out shopping, on her return she was told some other children had found the baby "choking" in her pram. On lifing the infant vomitus was seen in the mouth. Death took place about 1145 hours, 2 August 1958.

Autopsy findings. Well nourished and cared for. Small petechial haemorrhages over pleurae and thymus. There was general congestion, the trachea and main bronchi were full of a watery fluid with milk specks, similar to the contents of the stomach. The lungs were congested and oedematous, no consolidation was felt. There was a small patent ductus

arteriosus and both ovaries were cystic (weighing 2.4g on the right, 1.8g on the left).

Opinion. Asphyxia, inhalation of stomach contents.

Histological examination. The lungs showed congestion and acute emphysema with areas of haemorrhage (Fig 32). The bronchi showed some desquamation of the epithelium and a considerable small round cell infiltration of their walls. The alveolar walls were thickened and contained an infiltration of large and small mononuclear cells (Fig 33) and large mononuclear cells were often seen in alveolar spaces (Fig 34). A section stained by Gram's method showed gram positive cocci in short chains or diplococcal form in the bronchioles and in some alveoli. Elsewhere the organs showed congestion, with reactive follicular centres in the spleen. The ovaries showed multiple follicular cysts.

Conclusion. Acute bronchitis and momonuclear pneumonia mainly interstitial. Incidental findings: cysts of ovaries.

Case 140

Clinical details. Male aged 6 months. Found lying in the pram with his twin brother, and apparently underneath him, blue in the face, at 1900 hours, 4 August 1968. Artificial respiration was of no avail.

Autopsy findings. Cyanosis marked, especially of extremities. Scattered pleural petechiae. The trachea and main bronchi were full of thick yellow-white material similar to the stomach contents. The lungs were congested with some oedema. Remaining organs showed congestion.

Opinion. Asphyxia, inhalation of stomach contents.

Histological examination. The lungs showed gross congestion

with oedema and acute emphysema. The alveolar walls were thickened with an infiltration of macrophages, lymphocytes and polymorphonuclear cells, some of these were also seen in the alveolar spaces (Figs 35 and 36). A section stained by Gram's method showed scattered gram positive cocci often diplococcal or in short chains, with some clumps of large cocci resembling sarcina. The other organs showed congestion, with hyperplasia of the lymphoid follicles in the spleen. The liver showed vacuolisation of the cells.

Conclusion. Acute interstitial pneumonia.

Case 82

Clinical details. Female aged 8 months. Put to bed at 1830 hours, 18 June 1957, in the same room as another child. This other child was removed at midnight, the mother thought the infant was alright. She did not enter the room again until 1000 hours the next morning, to find the baby dead. The baby was normally fed when it cried about 0700 hours, but the mother apparently did not think it unusual that no crying occurred on this occasion. The medical officer who was called in found the windows of the room closed, the curtains drawn and the one radiator full on, too hot to touch. The temperature of the room was 98.5°F. The infant was lying on her back, clad in a loose smock, the face was pale and waxy and the oral temperature was 106.5°F.

Autopsy findings. The anterior fontanelle was open and there was a 2cm gap between the two frontal bones. The finger nails were cyanotic. There was white, frothy fluid between the lips and in the pharynx and this material filled the respiratory tree, the oesophagus and the stomach. There were a few petechiae in the pleura, the lungs showed basal congestion.

Opinion; Asphyxia following inhalation of vomitus.

Histology. None available. (Note: On review it was considered that the very hot room let to hyperpyrexia which was at least contributory to the death).

Case 17

Clinical details. Female aged 21 months. Found dead at 2100 hours, 5 May 1956, having been seen a short time previously, apparently all right.

Autopsy findings. Well nourished. Marked cyanosis. Numerous petechiae over the pericardium. There was a 3cm haematoma over the centre of the frontal region, but the brain underlying showed congestion only. The trachea and bronchi contained white milky fluid with particles, similar to the contents of the stomach. The lungs were congested and collapsed. The oesophagus contained stomach contents.

Opinion. Asphyxia: inhalation of regurgitated stomach contents.

Histological examination. The lungs were congested with some areas of acute emphysema and wide areas of collapse or consolidation (Fig 37). the bronchi showed disruption of their epithelium with exudate and large mononuclear cells in the lumen (Fig 38). The alveolar walls were thickened by an infiltration of mononuclear cells, large and small, and some of these were seen in the alveolar spaces (Fig 39). The other organs showed congestion.

Conclusion. Mononuclear pneumonia, mainly interstitial.

Serial 2B

B. Cases with Previous Mild Symptoms

Case 1

Clinical details. Female aged 5 weeks. The infant appeared to be well, gaining weight, and was changed from breast to carnation milk. For a week before death it appeared to have

abdominal colic, on the evening of 16 January 1956, it cried a great deal, but eventually settled and was put to bed. It was found dead just after midnight.

Autopsy findings. Marked cyanosis of extremities. Milk trickled from the nostrils on handling, the tip of the tongue protruded from between the lips. There were petechiae of the pleurae and pericardium with a little free blood in the pleural cavities. The larynx, trachea and bronchi contained large quantities of clotted milk. The lungs and all other organs were deeply congested.

Opinion. Asphyxia, inhalation of stomach contents.

Histological examination. The lungs showed widespread congestion and collapse with a few areas of acute emphysema. The bronchial epithelium was desquamated and the walls infiltrated with small round cells. The alveolar walls were thick, infiltrated with large and small mononuclear cells and the alveolar spaces contained large mononuclear cells in a little exudate (Figs 40 and 41).

Conclusion. Mononuclear pneumonia, mainly interstitial.

Case 14

Clinical details. Male aged 2 months. Seen by a medical officer because of a "running nose" and cough. The infant was slightly dyspnoeic, but there was no cyanosis nor abnormal signs in the chest. Linctus codeine was prescribed. At 2300 hours, 25 February 1956, the child was given a feed (bottle), it settled, then cried until 0200 hours next morning when it apparently settled again. The infant was found dead at 0930 hours with white frothy fluid over the face.

Autopsy findings. The extremities were cyanosed. Petechiae of the pleurae and pericardium. The respiratory tree contained

thick milky fluid similar to the stomach contents. The lungs and other organs were congested.

Opinion. Asphyxia, inhalation of vomitus.

Histology. None available.

Case 83

Clinical details. Male aged 2 months. Had been under treatment by a medical officer for a slight cold, but had apparently recovered. Well when seen by father at 0700 hours, but found dead by mother at 0830 hours, 27 June 1957. A feeding bottle partly filled with milk mixture was beside the baby, no vomitus was seen.

Autopsy findings. Well developed, well nourished infant, marked cyanosis of extremities. Some crusting of the left nostril. Numerous petechiae in pleurae and pericardium and thymus. The trachea and bronchi were filled with milky fluid similar to the moderate quantity of stomach contents. The lungs were congested. Petechiae were also seen under the capsule of the right kidney and all organs were congested. The ductus arteriosus was patent, admitting a large probe.

Opinion. Asphyxia consequent on inhalation of milk.

Histological examination. The lungs showed severe congestion with areas of oedema, haemorrhage and acute emphysema. The bronchi showed desquamation of their epithelium (Fig 42), the alveolar walls were thickened and the alveoli were full of exudate and cells (Fig 43). In areas this infiltration consisted of large mononuclear and polymorph cells (Fig 44), in others it consisted of small round cells and polymorphs (Fig 45).

Conclusion. Pneumonia, predominantly mononuclear in type.

Case 159

Clinical details. Male aged 3 months. Had been treated about 3 weeks previously by a medical officer for diarrhoea, the mother being told to report back if necessary, but she did not do so. The infant appeared to be progressing though the stools were still loose and frequent (5 per day). The child was fed (bottle) at 0600 hours, 4 January 1959, the parents went back to bed and awoke at 1100 hours to find the baby dead. They had not realised the infant was ill and had taken him regularly to the clinic. It was reported that the parents (Canadian) were living in poor conditions on the German economy.

Autopsy findings. A rather thin infant (weight 8lbs 10ozs) with some dehydration including depression of the anterior fontanelle. There were petechiae of the pericardium and thymus. The respiratory tree contained moderate quantities of milk feed similar to the contents of the stomach. The lungs were congested. There was congestion of all the organs including the intestinal tract which showed conspicuous congested lymphoid patches especially in the lower iteum.

Opinion. Asphyxia due to inhalation of stomach contents. There was evidence of intestinal inflammation which, by dehydration and toxaemia, may have contributed to the death.

Histological examination. The lungs were congested with areas of acute emphysema. The bronchioles showed desquamation of their epithelium and the alveoli showed some thickening of their walls with exudate and large mononuclear cells in the alveolar spaces (Figs 46 and 47). A section stained by Gram's method showed scattered gram negative cocci in pairs and short chains. The mesenteric lymph nodes were congested and showed

reticulum cell activity and some plasma cells, the small intestine showed oedema of the mucosa with a plasma cell infiltration. The kidneys showed swelling of the glomerular tufts.

Conclusion. Enteritis and early mononuclear pneumonia.

Case 59

Clinical details. Female aged 4 months. This infant had a cold, but the mother was not worried about her condition. She was put to bed at 2030 hours, 26 January 1957, and at 0115 hours found lying face down, blue in colour. The doctor who was summoned found it dead. The mouth was full of frothy fluid.

Autopsy findings. A normally developed, well nourished infant. Extremities deeply cyanosed; froth on the lips. Petechiae in pleurae, pericardium and thymus (the latter was large, weighing 25g). The larynx was obstructed by a bolus of firm clotted milk, 1 inch in diameter, but the trachea was empty.

Opinion. Asphyxia: blockage of airway by regurgitated food.

Histological examination. The lungs were congested. The bronchi showed partial epithelial denudation with bacterial clumps and an infiltration of small mononuclear and polymorph cells in their walls (Fig 48). In areas the alveolar walls were thickened, with numerous large mononuclear cells in the lumen (Figs 49 and 50), some of these being multinucleated (Fig 51). In other areas the infiltration consisted of small round cells and polymorphs (Fig 52).

Opinion. Pneumonia, mixed broncho- and mononuclear cell.

Case 120

Clinical details. Male aged 8 months. The evening before death he had been vomiting. Found next morning 20 February 1958, very still with eyes fixed. The medical officer summoned

found the infant was dead, flat on its back, with considerable cyanosis of the face.

Autopsy findings. Well developed and well nourished. Anterior fontanelle large. Petechiae of pleurae, pericardium and thymus, the latter weighing 23g. The oesophagus contained partly digested milk and this material nearly filled the trachea and main bronchi, the mucosa of which was intensely congested. The lungs and other organs were congested and there were massive bilateral adrenal haemorrhages.

Opinion. Asphyxia due to inhalation of vomitus. There may have been some underlying acute infective condition.

Histological examination. The trachea showed acute congestion with oedema and partial desquamation of its epithelium, the corium of the mucosa being infiltrated by plasma cells and some macrophages (Fig 53). The lungs were congested with areas of emphysema and collapse (Fig 54). The bronchi showed desquamation of their lining cells, leading to disruption in some, and the shed epithelium was mixed with macrophage cells (Fig 55). The alveolar walls were thickened and infiltrated with mononuclear cells and polymorphs which were also seen in the alveolar lumen (Fig 56). Other organs were congested, with haemorrhage into the adrenals, prominent reactive hyperplasia of the follicles of the spleen and prominent groups of islet cells in the pancreas.

Conclusion. Acute tracheo-bronchitis and commencing pneumonia.

Serial 2C

Case 103

C. A Case Dying in the Presence of an Adult

Clinical details. Female aged 6 months. The infant had been unwell, with a slight cough, but the parents were not worried

about its condition and did not seek medical advice. She was fed at 1800 hours, 21 October 1957, and seemed to settle, but was heard to cough at 2100 hours. The parents went to see it, it vomited in their presence, then choked and turned blue. Despite artificial respiration the infant was dead when the medical officer arrived.

Autopsy findings. Somewhat undernourished. Petechiae of the pleurae and pericardium. The larynx, trachea and bronchi were full of milky yellow fluid similar to the contents of the stomach. The lungs were congested, the right upper lobe was firm. The remaining organs showed congestion only.

Opinion. Asphyxia due to inhalation of vomitus. (Possible pneumonia of right upper lobe in addition).

Histological examination. The lungs throughout showed practically no aereated tissue, all sections examined being consolidated. The large bronchi showed partial desquamation of their epithelium (Fig 57), the smaller ones often contained pus (Fig 58), and some were partly disorganised by this acute inflammatory change forming incipient abscesses (Fig 59). In areas the consolidation was due to a mononuclear cell infiltration of the thickened alveolar walls and the alveolar lumen (Figs 60 and 61), some of these mononuclear cells being foamy in character (Fig 62). In other areas there was a polymorphonuclear cell infiltration (Figs 63 and 64), while in still other areas there was a mixed picture (Fig 65) including polymorphs, mononuclear and giant cells. The surface of the lungs showed a fibrinous pleurisy (Fig 66).

Conclusion. Acute broncho-pneumonia and mononuclear pneumonia.

Serial 2D

Case 171

D. A Case Dying After a Brief Acute History

Clinical details. Male aged 6 months. This infant had been in apparent good health until 0745 hours, 22 March 1959, when it cried, coughed, choked and went blue. It appeared to be in a coma for the next three-quarters of an hour when he was admitted to a German Hospital, cyanosed with a weak pulse. The trachea was aspirated and oxygen given, but it died 5 minutes after admission. While mouth to mouth respiration was being carried out a quantity of milky fluid came down one nostril.

Autopsy findings. Cyanosis of lips. The larynx and trachea were empty but the bronchi, which showed congested walls, contained white viscid fluid similar to the contents of the stomach. The lungs were deeply congested with little aereation noticed.

Opinion. Asphyxia: inhalation of vomitus.

Histological examination. The lungs were congested and oedematous with patchy collapse and oedema (Fig 67). The large bronchi in areas showed loss of the epithelial lining, with congestion of the walls and an infiltration of small and large mononuclear cells including some plasma cells (Fig 68). The alveolar walls were thickened by congestion and an infiltration of mononuclear cells and some polymorphs (Fig 69) and a number of alveoli showed a hyaline membrane (Fig 70). The suprarenals showed areas of haemorrhage.

Conclusion. Bronchitis and pneumonia associated with hyaline membrane formation.

3. INFANTS IN WHOM AUTOPSY SHOWED MACROSCOPIC EVIDENCE OF PNEUMONIA OR UPPER RESPIRATORY INFECTION

Serial 3A

A. Cases with no Previous Symptoms

Case 33

Clinical details. Female aged one month. Had thrived, seen by mother at midnight 24/25 August 1956, apparently well; given a bottle teat to suck as a "dummy". Found dead by the mother next morning. When seen by a medical officer the infant was lying on the right side, the head on a soft pillow which was not occluding the air passages.

Autopsy findings. Well nourished. The congested lungs showed scattered areas of consolidation, otherwise examination of the body showed nothing of note beyond general congestion.

Opinion. Broncho-pneumonia.

Histological examination. The lungs showed intense congestion with some acute emphysema. Most of the small bronchi and bronchiolar showed desquamation or disintegration of their lining epithelium (Fig 71). The alveolar walls were thickened and they, and the lumen of the alveoli, were infiltrated by large and small mononuclear cells and polymorphs (Figs 72 and 73). A section stained by Gram's method showed gram positive diplococci with some short chains and clumps. Remaining organs were congested, the regional lymph nodes show an infiltration with macrophages and there were a few scattered polymorphs in the liver.

Conclusion. Fulminant pneumonia.

Case 127

Clinical details. Female aged 3 months. Premature at birth (weight 3 lbs 3 ozs) but thrived and on discharge from hospital 7 weeks later weighed 8 lbs. No history of respiratory infection, fed at 1530 hours, 10 April 1958, and found dead in

her pram at 1900 hours.

Autopsy findings. Well developed, well nourished. Crusted brown material in nose. Petechiae of pleurae and pericardium. Bronchi contained some frothy, brown mucoid material. The lungs were congested, and small white beads of fluid could be expressed from the smaller bronchi. Remaining organs congested.

Opinion. Asphyxia due to an acute upper respiratory tract infection.

Bacteriological examination. A mixed growth of a Friedlander's bacillus and a coliform organism was obtained from a lung swab.

Histological examination. The lungs showed congestion with patchy areas of collapse and emphysema. Small bronchi showed commencing epithelial desquamation and their walls were infiltrated with a moderate number of small round cells (Fig 74). The alveolar walls were thickened by the intense congestion and there were scattered large mononuclear cells in the alveolar spaces (Figs 75 and 76). The remaining organs showed congestion only.

Conclusion. Bronchitis and early acute mononuclear pneumonia.

Case 115

Clinical details: Male aged 4 months. Premature at birth (weight 3lbs 14ozs), discharged when 6 weeks old, weight 5lbs 15ozs, and general condition good (there was a mild eczema present). However, some 2 months later the weight was only 6lbs 12ozs; medical advice was not sought. The infant was found dead on the morning of 3 February 1958.

Autopsy findings: A poorly nourished infant, 6lbs 5ozs in weight, with wrinkled skin showing loss of elasticity and practically no subcutaneous fat. The limbs were particularly

emaciated. The head was dilolocephalic, both fontanellas were open and depressed. The skin in the nappy area showed a number of acute and chronic ulcers. There was some vomitus in the oesophagus and respiratory tree, but insufficient to occlude the lumen. Bilateral pleural petechiae were noticed and there was a small pleural effusion on the left side. The lungs were congested with consolidation at the apex of the right lung and of the right lower lobe. The intestines were nearly empty and their walls very thin.

Opinion: Pneumonia in a marasmic infant showing signs of neglect.

Histological examination: The lungs showed congestion with patchy consolidation. The bronchi showed desquamation of their lining epithelial cells (Fig 77) with a surrounding infiltration of polymorphs which in areas filled the alveoli and infiltrated the alveolar walls (Fig 78). In some areas this infiltration was more mononuclear in type (Fig 79). There were scattered gram-positive diplococci (Fig 80). Remaining organs were congested, with reactive follicles in the spleen, a slight polymorph infiltration of the liver and haemorrhage into the adrenal glands.

Conclusion: Broncho-pneumonia with areas mononuclear in type.

Case 203

Clinical details: Male aged 4 months. This infant appeared normal when it was fed at 1330 hours on 29 October 1959. The mother saw it at 1500 hours, when nothing appeared amiss. When she went to give the child a feed at 1730 hours, however, she found it completely under the sheets and blankets which were stained with vomitus. A medical officer pronounced it dead.

Autopsy findings: The lungs and other organs were congested, there was no inhaled vomitus but the respiratory tree contained mucopurulent material which could be squeezed from the cut smaller bronchi.

Opinion: Asphyxia from fulminant respiratory infection.

Bacteriological examination: The exudate from the trachea yielded a growth of Streptococcus pneumoniae.

Histological examination: The lungs were congested with widespread consolidation, only scanty alveoli being aerated. The trachea showed desquamation of its lining cells and a considerable infiltration of the congested wall by small round cells and polymorphs (Fig 81), the bronchi showed the same features. The alveolar walls were thickened and infiltrated by similar cells, the alveolar spaces contained in areas large mononuclear cells, sometimes giant cells (Fig 82). The remaining organs showed congestion and the liver some residual haemopoetic tissue.

Conclusion: Acute tracheo-bronchitis and pneumonia.

Case 225 Clinical details: Male aged 5 months. Appeared normal when fed at 0900 hours, 22 February 1960. Mother found it dead at 1200 hours.

Autopsy findings: Well nourished. There was general congestion. The respiratory tree contained much purulent material, the lungs were markedly congested with consolidation of the upper and middle lobes of the right lung and of the lower lobe of the left.

Bacteriological examination: Films from the bronchi showed an organism resembling a streptococcus and swabs from the

tracheal pus yielded a mixed growth of a beta-haemolytic streptococcus and a Friedlanders' bacillus.

Opinion: Acute streptococcal pneumonia.

Histology: None available.

Case 57

Clinical details: Male aged 6 months. The child was in previous good health and was found dead early on the morning of 25 January 1957. The medical officer called in at 0745 hours, found the infant lying in a cot on its left side; there was no evidence of vomitus.

Autopsy findings: Well nourished and well cared for. The bronchi contained pus, the lungs were congested and felt firm, oedema fluid and pus being expressed from the cut surface, especially from the left upper and right lower lobes.

Opinion: Broncho-pneumonia.

Histological examination: The lungs were congested, with areas of collapse, acute emphysema and consolidation (Fig 83). The bronchi showed some epithelial desquamation with mononuclear and polymorph cells in the walls. The alveolar walls were thickened and contained large and small mononuclear cells and polymorphs, the alveolar spaces containing the large type (Figs 84 and 85).

Conclusion: Pneumonia: Interstitial and mononuclear.

Case 166

Clinical details: Female aged 9 months. Had been previously well, found dead in bed in the morning of 28 February 1959.

Autopsy findings: Petechiae of pericardium, thymus and brain. Frothy fluid in larynx. Mucosa of trachea and bronchi congested with mucopurulent material in left main bronchus. Lungs firm and congested.

Opinion: Asphyxia secondary to an acute pneumonia.

Histology: None available.

Case 215

Clinical details: Male aged 21 months. This child had been seen often by medical officers in the past with difficulty in breathing and excessive crying, but had not been unwell immediately before death. It awoke one evening and was given a glass of cold milk and the mother went back to sleep. On awakening at 0830 hours, 14 January 1960, she found the infant dead.

Autopsy findings: The trachea and bronchi contained mucopurulent material and the lungs showed scattered areas of consolidation throughout, pus being expressed from the smaller bronchi. Otherwise the examination revealed only congestion.

Opinion: Broncho-pneumonia.

Histological examination: Confirmed the naked-eye diagnosis (no slides remain for photography).

Conclusion: Broncho-pneumonia.

Case 246

Clinical details: Male aged 23 months. Found dead in bed, 22 June 1960, no previous history of note.

Autopsy findings: Tonsils were enlarged with an exudate and there were enlarged lymph nodes in the neck. Petechiae were noted in the mediastinum, pleurae, pericardium, thymus, the latter was large. The trachea was intensely congested and the bronchi contained frothy mucus. The lungs showed patchy consolidation with red hepatisation.

Opinion: Asphyxia from acute broncho-pneumonia.

Histological examination: The lungs showed widespread congestion and patchy oedema. The bronchi showed a marked peribronchial infiltration with polymorphs and small round cells (Fig 86), and some showed complete loss of their

epithelium with scanty polymorphs and large and small mononuclear cells in the wall, (Fig 87). The remaining organs showed congestion, with reactive lymphoid follicles in the spleen, reactive changes and a moderate polymorph and plasma cell infiltration of the tonsils, reactive changes and polymorphs in the cervical lymph nodes and a few scattered polymorphs in the liver.

Conclusion: Tonsillitis, acute cervical lymphadenitis and early pulmonary infection.

Serial 3B

B. Cases with Previous Mild Symptoms

Case 16

Clinical details: Male aged 2 months. The day before death appeared to have earache, but was apyrexial. Found dead, lying face down, in his cot on the morning of 27 April 1956.

Autopsy findings: Cyanosis of finger and toe nails. Middle ears normal. Slight quantity of pinkish froth in the respiratory tree. The lungs were congested with areas of patchy collapse plus poor aereation. Remaining organs congested.

Opinion: Probably fulminating broncho-pneumonia.

Histological examination: The lungs showed marked congestion with areas of collapse and consolidation (Figs 88 and 89), the latter showing some areas where the bronchioles were completely disrupted by these inflammatory cells, forming incipient microabscesses (Fig 90).

Conclusion: Acute broncho-pneumonia.

Case 116

Clinical details: Male aged 2 months. History of having a heavy cold, with pyrexia, for 24 hours. Mother was suffering from influenza and the medical officer considered the child

also had this condition; no treatment was considered necessary and no anxiety was felt. The child was found dead next morning, at 0900 hours on 5 February 1958, lying face down with its head on the soft pillow.

Autopsy findings: Well nourished infant with cyanosis of extremities and face. A few petechiae on pleurae. Mucopurulent material in trachea and main bronchi, lungs congested with patchy areas of bronch-pneumonia consolidation, this purulent material could be expressed from these areas which were especially marked over the middle lobe of the right lung and the lower lobe of the left.

Opinion: Broncho-pneumonia.

Histology: None available.

Case 153 Clinical details: Female aged 9 weeks. This infant had a slight cough 4 days before death, but when seen at the clinic appeared well. On the evening before death she was listless and felt hot, a medical officer examined her at 0130 hours, 15 October 1958, found that she was pyrexial, but nothing else abnormal was discovered. The infant was fed at 0200 and 0400 hours and took the feeds well. She was found dead at 0700 hours with vomitus on the clothes and blankets.

Autopsy findings: There was a slight pink macular rash over the forehead and trunk. The trachea contained a little regurgitated food, but there was no question of obstruction by this. The congested lungs showed patches of consolidation with a fibrinous exudate over the pleura and small pleural effusions. Pus could be expressed from the fine bronchi. Both adrenals were haemorrhagic.

Opinion: Broncho-pneumonia and pleurisy with bilateral adrenal

haemorrhage.

Histological examination: The lungs showed marked congestion with desquamation of the epithelium of the smaller bronchi (Fig 91) and widespread consolidation (Fig 92). The predominant inflammatory cells were of the large mononuclear type, there were a few polymorphs (Fig 93) and organisms were visible. With a Gram's stain these were seen to be short gram negative rods, some diplo-bacillary and some encapsulated, morphologically resembling Friedlander's bacillus. Remaining organs showed congestion, with haemorrhages in the adrenals.

Conclusion: Acute mononuclear pneumonia, probably Friedlander's, with secondary adrenal haemorrhage due to toxaemia.

Case 164

Clinical details: Female aged 3 months. Had thrived since birth, but had been coughing for a day or two. Put to bed as usual one night, apparently well, found dead in the morning of 14 February 1959.

Autopsy findings: Well nourished. Deep cyanosis. The pleurae and pericardium showed a few petechiae. The respiratory tree contained pink frothy material and the congested lungs felt practically airless. Remaining organs showed congestion.

Opinion: Pulmonary oedema probably secondary to an acute pneumonia.

Histological examination: The trachea showed desquamation of its epithelium in areas with an underlying infiltration of the mucosa by mononuclear cells including plasma cells (Fig 94); these changes were even more marked in the bronchi (Fig 95).

The alveolar walls were thickened by congestion and small round cells, the alveolar spaces contained large mononuclear cells (Fig 96). Remaining organs showed congestion with reactive lymphoid hyperplasia of the splenic follicles.

Conclusion: Acute tracheo-bronchitis and mononuclear pneumonia.

Case 77

Clinical details: Male aged 3½ months. Well until the evening of 10 June 1957, when the infant started vomiting at 2030 hours. A medical officer called at 2215 hours and found the baby dead, with vomitus soiling the face.

Autopsy findings: There was fine white frothy material in the mouth, nostrils and posterior nares. The bronchi contained purulent material, the pleural surfaces were irregularly mottled and the cut surface of the lung showed peribronchial congestion and a purulent exudate could be expressed from the bronchi.

Opinion: Pneumonia. No evidence of inhaled vomitus.

Histology: None available.

Case 210

Clinical details: Male aged 3 months. This infant had a severe gastro-enteritis at the age of one month, but had been well since until the evening of 16 December 1959, when it commenced to vomit. The infant appeared quite unresponsive at 0730 hours next morning and a medical officer found it was dead with slight frothing at the mouth.

Autopsy findings: Petechiae of the dura, pleurae, pericardium and thymus. The respiratory passages were clear, the lungs were congested and showed consolidation of both lower lobes; pus could be expressed from the bronchi. Remaining organs were congested with some cerebral oedema.

Opinion: Asphyxia due to pneumonia.

Histological examination: The bronchi showed epithelial desquamation, the lumen containing blood as well as desquamated cells (Fig 97). The lungs showed collapse and consolidation with some emphysematous alveoli (Fig 98), the alveolar walls were thickened and infiltrated with small and large mononuclear cells with some polymorphs, the alveolar spaces containing exudate and similar cells (Fig 99). Remaining organs showed congestion with reactive follicular centres in the spleen and haemorrhage in the adrenals.

Conclusion: Acute pneumonia, mainly interstitial.

Case 52

Clinical details: Female aged 4 months. This infant had had diarrhoea for a day, having had an attack of "bronchitis" one week before. It whimpered from midnight to 0300 hours, 18 December 1957, and was found dead at 0700 hours.

Autopsy findings: Well nourished. The respiratory tree contained mucoid material. The congested lungs had patchy areas of consolidation throughout, being particularly marked in the left lower lobe.

Opinion: Broncho-pneumonia.

Histology: None available.

Case 252

Clinical details: Female aged 5 months. Had a cold "on and off" for one week, but no anxiety aroused. The infant was fed at 0400 hours, 6 July 1960, and found dead by the parents at 0930 hours. There was a little vomitus on the pillow and the child was blue.

Autopsy findings: Somewhat obese infant. The fauces were congested, the tonsils enlarged and there was marked congestion of the trachea and bronchi, the former being purple in colour.

The bronchi contained frothy white material. The lungs were congested and firm, the cut surface being mottled red and purple. The middle ears contained pus. Remaining organs showed congestion. There was a patent ductus arteriosus, 0.1cm in diameter. The brain showed small cysts up to 0.3cm in diameter, containing clear fluid, in the region of the lenticular necleus of the right cerebral hemisphere.

Opinion: Bilateral pneumonia and upper respiratory tract infection. Small patent ductus arteriosus.

Histological examination: The lungs were congested with areas of acute emphysema, consolidation and peribronchial cellular infiltration. The bronchi showed epithelial desquamation (Fig 100) with considerable infiltration of the walls and lumen by inflammatory cells, mainly polymorphonuclear, disrupting the architecture in areas (Figs 101 and 102). The alveolar walls were thickened with an infiltration of small round cells and polymorphs, while the lumen contained large mononuclear cells; sometimes giant cells were seen (Fig 103). The brain showed small cysts with reactive gliosis in the region of the lenticular nuclei. The remaining organs showed congestion.

Conclusion: Tracheo-bronchitis and pneumonia. The aetiology of the brain cysts is obscure, but they are interpreted as probably being the end result of cerebral birth injury.

Case 60

Clinical details: Female aged 6 months. Two weeks before death the infant was unwell with some coughing, but the medical officer consulted found no obvious illness and two days later it had apparently recovered. Four days before death

coughing recurred, with refusal of feeds and a cough mixture was prescribed. The child appeared to improve and was normal the day before death. The infant became restless at 0200 hours, then slept and was found dead, lying on her back, at 0755 hours, 28 January 1957.

Autopsy findings: Normal development and well cared for infant. Some dried vomitus around the mouth. Trachea and bronchi contained a small quantity of sticky purulent material. The lungs were congested and oedematous, with multiple small areas of collapse in both, and purulent material could be expressed from the small bronchi.

Opinion: Fulminating broncho-pneumonia.

Bacteriological examination: A swab from the left lower lobe yielded a heavy growth of a Staphylococcus pyogenes.

Histological examination: The lungs showed intense congestion with some interstitial haemorrhage and areas of emphysema. The bronchial walls showed denudation of the epithelium and an underlying infiltration with mononuclear cells accompanied by clumps of organisms (Fig 104). The alveolar walls were thickened and showed small round cells, some in alveolar spaces. A section stained by Gram's method showed clumps and chains of gram positive cocci morphologically resembling a staphylococcus and some large gram positive bacilli.

Conclusion: Bronchiolitis and early pneumonia probably staphylococcal in origin.

Case 61

Clinical details: Male aged 6 months. This infant had had previously several mild chest infections, none serious. On the morning of death a medical officer was called in because the infant had a cold and was "chesty". He found a pyrexia of

101°F, signs of bronchitis and prescribed aspirin, linctus and penicillin. He did not view the case with concern. In the early evening of 11 February 1957, a series of convulsions occurred and the baby died shortly after admission to a German hospital.

Autopsy findings: Normal development. Cyanosis of nails and lips. Nose crusted with dried pus. Early right otitis media. Petechiae of pericardium. The pharynx and respiratory tree were inflamed and the trachea and bronchi contained sticky pus. The lungs were congested with firm areas and pus could be expressed from the small bronchi. Remaining organs congested except the liver which appeared to be fatty.

Opinion: A severe fulminating respiratory infection.

Bacteriological examination: A swab from the right upper lobe yielded a growth of Staphylococcus pyogenes and the same organism, with a coliford bacillus in addition, was isolated from the pus in the respiratory tree.

Histological examination: (Slides no longer available for photography). The lungs were congested with areas of collapse and consolidation. The bronchi showed epithelial desquamation and their walls were infiltrated with polymorphs. A Gram-stained section showed organisms morphologically resembling staphylococci.

Conclusion: Acute staphylococcal broncho-pneumonia.

Case 220

Clinical details: Male aged 7 months. The infant was fretful and feverish one evening. At 0330 hours next morning, 24 January 1960, it was found blue and appeared to have difficulty in breathing; it died a few minutes later.

Autopsy findings: Well nourished. Deeply cyanosed. Petechiae of the conjunctiva, meninges, pericardium, stomach, mesenteric nodes, kidney and pleurae. The mucosa of the respiratory tree was inflamed and contained pus. The lungs were deeply congested, with only patchy aeration and pus could be expressed from the bronchi. The adrenals were haemorrhagic, the brain oedematous and other organs showed congestion.

Opinion: Broncho-pneumonia, with probable septicaemia.

Bacteriological investigation: Swabs from the respiratory tract yielded a heavy growth of a beta-haemolytic streptococcus.

Histological examination: (Material no longer suitable for photography). The lungs were congested and oedematous with areas of collapse and consolidation. The bronchi showed desquamation of their epithelium with an infiltration of small round cells in the walls. The alveolar walls were thick, infiltrated with large and small mononuclear cells and the alveolar spaces contained exudate and similar cells. The remaining organs were congested with reactive hyperplasia of the follicles of the spleen and haemorrhage into the adrenals.

Conclusion: Broncho-pneumonia, mononuclear in type, probably streptococcal in origin.

Case 132

Clinical details: Female aged 18 months. This child was well until the day before death when she vomited, a medical officer found her pyrexial at 1010 hours, 23 May 1958, with some tachycardia (pulse rate 120 per minute), but no localising signs. He said he would return that afternoon, but the child died suddenly at 1400 hours.

Autopsy findings: Petechiae of brain and pericardium, pharynx, larynx, trachea and bronchi congested and the latter contained

thin yellow purulent fluid. There was considerable pulmonary congestion.

Opinion: Asphyxia probably secondary to acute pneumonia.

Bacteriological investigation: Swabs from both main bronchi yielded a fairly heavy growth of Staphylococcus pyogenes.

Histological examination: The lungs were congested with areas of acute emphysema. The bronchi showed small round cells and polymorphs in their walls (Fig 105) and large mononuclears and polymorphs mixed with the desquamated epithelium in their lumen (Fig 106). There were areas of early consolidation, with thickening of alveolar walls and an infiltration of inflammatory cells, mainly peribronchial (Fig 107). A Gram-stained section showed gram-positive cocci in diplococcal and short chain formation.

Conclusion: Acute bronchitis and bronchiolitis with commencing broncho-pneumonia.

Serial 3C

Case 114

C. Cases Dying in the Presence of an Adult

Clinical Details: Male aged 2 months. Child thriving until 2 days before death when it started coughing and vomiting. A medical officer examined the infant at 2120 hours, the temperature was 98.6°F, there was no cyanosis. There were occasional scattered rhonchi and crepitations in the right side of the chest. A diagnosis of acute bronchitis was made and penicillin prescribed. The doctor was not unduly worried about the child's condition. For the next day or so it sometimes appeared normal, sometimes had difficulty in breathing. The father saw the child at 0730 hours, 20 January 1958, and in his presence it suddenly stopped breathing and was found to be dead.

Autopsy findings: Well developed and well nourished. Marked cyanosis of extremities. Petechiae of the pleurae. The pleural cavities contained small effusions of clear fluid. The trachea and bronchi contained tenacious muco-pus. Both lungs were congested and firm, on squeezing small beads of pus could be expressed from the small bronchi. Elsewhere the organs were congested.

Opinion: Broncho-pneumonia.

Bacteriological investigation: Swabs from the main bronchi yielded a growth of a penicillin-resistant Friedlander's bacillus. The pleural fluid was sterile.

Histological examination: The lungs were congested with patchy areas of consolidation. The bronchi showed in areas desquamation of their epithelium and intense surrounding inflammatory reaction in a number of areas (Fig 108). In some areas the alveolar walls were thickened with an infiltration of small round cells and a few polymorphs, the alveolar spaces contained large mononuclear and giant cells (Figs 109 and 110). The remaining organs were congested, the regional lymph nodes in the hilar regions showed an infiltration of large macrophage cells and polymorphs.

Conclusion: Acute broncho-pneumonia and mononuclear pneumonia.

Case 238

Clinical details: Male aged 7 weeks. The child had apparently been well, but suddenly turned blue and unresponsive. A civilian doctor was called in at 1200 hours, 9 April 1960, and found a comatose infant who died very shortly afterwards despite attempted resuscitation.

Autopsy findings: There was no evidence of inflammation of the upper respiratory tract, but the congested lungs showed areas

of broncho-pneumonic consolidation and of oedema, and thin pus could be expressed from the smaller bronchi. The foramen ovale was patent and the left kidney showed a number of cysts, otherwise the remainder of the examination showed congestion only.

Opinion: Acute broncho-pneumonia (incidental findings - patent foramen ovale and congenital cysts of left kidney).

Bacteriological investigation: A mixed growth of Streptococcus viridans and a Friedlander's bacillus was obtained from swabs of both the right and left bronchus.

Histological examination: The lungs were congested and showed areas of emphysema. The bronchial epithelium was in the main intact, the walls showed an infiltration of polymorphs (Fig 111). There were many areas of consolidation with thick alveolar walls, infiltrated by large and small mononuclear cells, polymorphs and plasma cells with large mononuclears predominant in the alveolar spaces (Figs 112 and 113). The cysts seen macroscopically in the kidney are greatly dilated calyces of the pelvis of a congenital hydronephrosis.

Conclusion: Interstitial pneumonia (incidental finding - left congenital hydronephrosis).

Serial 3D

D. Cases Dying after a Brief Acute History

Case 161

Clinical details: Male aged 5 weeks. This baby had been thriving, but on the day of death developed diarrhoea. On examination in the morning a medical officer found a normal temperature, the chest and abdomen showed no abnormal physical signs and a diagnosis of mild gastro-enteritis was made, but as the mother did not appear capable of looking after the

infant properly, it was admitted to hospital. On examination at 1530 hours, 28 January 1959, there was no evidence of clinical dehydration, the breathing was noisy but the chest sounds clear. There was no apparent cause for concern, but the baby stopped breathing suddenly at 1815 hours and shortly afterwards the heart stopped beating despite resuscitative measures.

Autopsy findings: A somewhat thin baby. Petechiae of pleurae, pericardium and peritoneum. The respiratory passages were empty. The lungs and pleurae were intensely congested and both lower lobes were consolidated. The central part of the small intestine was congested and there was a haemorrhage in the right adrenal gland.

Opinion: Bilateral lobar pneumonia (with evidence of enteritis).

Histological examination: (The slides are no longer available for photography). The lungs were congested with areas of collapse and emphysema. The walls of some bronchi showed epithelial desquamation and were infiltrated with small round cells. The alveolar were thickened and infiltrated with small and large mononuclear cells, some alveolar spaces contained exudate and macrophages. A section stained by Gram's method showed gram-positive diplococci morphologically resembling Streptococcus pneumoniae. The intestine showed some polymorph and macrophage infiltration of the mucosa. Remaining organs showed congestion with haemorrhage into the adrenals.

Conclusion: Interstitial pneumonia. Enteritis.

Case 167

Clinical details: Male aged five months. On 1 March 1959, this infant was listless and would not take its feed. It was examined by a medical officer at midday and found to be

cyanotic, with rapid respirations and signs of dehydration. The pulse was weak and the rectal temperature 107°F. The child was immediately transferred to hospital, but was dead on arrival.

Autopsy findings: The organs showed general congestion. There were petechiae in the pleurae. There was a quantity of yellow fluid in the right pleural cavity. The lungs were grossly congested. The cerebrospinal fluid was under increased pressure.

Opinion: Acute broncho-pneumonia.

Bacteriological investigation: A Friedlander's bacillus was isolated from the cerebro-spinal fluid, the pleural fluid and a lung swab.

Histological examination: (Slides are no longer adequate for photography). The lungs are congested with small areas of acute emphysema and widespread collapse and consolidation. The bronchi show desquamated epithelium with admixed exudate and mononuclear cells. The alveolar walls are thickened by marked congestion and the presence of large mononuclear cells, some of which are seen in alveolar spaces. The other organs showed congestion, with reactive hyperplasia of the follicles of the spleen and reticulum cell hyperplasia and polymorph infiltration of the hilar lymph nodes. A section stained by Gram's method shows numerous gram-positive cocci morphologically resembling a staphylococcus.

Conclusion: Interstitial pneumonia.

Case 248 Clinical details: Male aged 2 months. The infant had seemed to be well, but "all of a sudden turned purple" on 16 June 1960. It was rushed to a clinic but no heart beat could be felt and resuscitation was of no avail.

Autopsy findings: Well nourished. The trachea contained thick pus, the congested lungs showed no definite consolidation but pus could be expressed from the small bronchi.

Opinion: Acute broncho-pneumonia.

Histological examination: The lungs were congested and showed areas of acute emphysema. The bronchi showed desquamated epithelium (Fig 114). Some alveolar walls were thickened and contained large mononuclear cells which were also seen in alveolar spaces (Fig 115).

Conclusion: Acute interstitial pneumonia.

Case 118

Clinical details: Female aged 2 months. This infant was put to bed after its evening feed, apparently normal. At 0100 hours, 8 February 1958, the mother noticed that the infant's breathing was extremely rapid, her colour was grey and there was profuse sweating. A medical officer summoned diagnosed acute bronchitis, but the child died before transport to hospital could be arranged.

Autopsy findings: A plump, well developed infant with pronounced lividity of the dependant portions. There was widespread congestion of all organs. The trachea and main bronchi contained a little vomitus, but no obstruction, their mucosal surfaces were intensely congested. The lungs were congested with nunerous haemorrhagic areas.

Opinion: Acute tracheo-bronchitis.

Bacteriological examination: A large gram-positive organism was isolated from the lung and examined at the Royal Army Medical College. It was a non-sporing, non-encapsulated motile rod, growing in nutrient agar at 20°C. The following sugars were fermented with the production of gas: glucose,

maltose, lactose, saccharose, mannite and dulcite. Salicin was not fermented. The organism was Indole +, MR +, VP -, H_2O production + and did not split urea. There was no growth in Koser's citrate medium nor liquefaction of gelatin. It was catalase +.

Opinion: This organism is not a member of the genus Bacillus, neither is it a lactobacillus. Its identity remains obscure.

Histological examination: The trachea showed complete necrosis of the mucosa with haemorrhage, but no inflammatory infiltration of the wall (Fig 116). The lungs showed gross congestion and oedema with areas of haemorrhage (Fig 117). The bronchi showed disruption, the lumen containing exudate and desquamated epithelial cells (Fig 118). The alveolar walls contained mononuclear cells which were also seen in the spaces (Fig 119). In some areas there were numerous cystic spaces not related to air passages and with no epithelial lining - these were interpretated as being post-mortem artefacts due to production of gas by the large gram-positive organisms present particularly in these areas. Remaining organs showed congestion.

Conclusion: Haemorrhagic pneumonia. (The organism isolated does not resemble Bacillus anthracis)

Case 12

Clinical details: Female aged 4 months. This child had had a "cold" for some days and had been off her feeds. A sibling aged 8 years had measles at this time. The infant became wheezy and was admitted to hospital at 1020 hours, 2 November 1956, where it was found to be pyrexial ($104^{\circ}F$) with signs of a chest infection. It suddenly collapsed in total respiratory obstruction 4 hours later and died despite efforts at resuscitation.

Autopsy findings: Cyanosed extremities. There was a general congestion of all organs. The mucosa of the respiratory tree was intensely congested, there was a bilateral pleural effusion and the lungs showed areas of consolidation. The bronchi contained tenacious green mucus.

Opinion: Respiratory failure due to broncho-pneumonia.

Histological examination: The lungs showed general congestion with desquamation of bronchial epithelium, thickened alveolar walls and exudate containing cells in the alveolar spaces (Fig 120). The cellular infiltration consisted of small round cells and some polymorphs in the walls and large mononuclears, sometimes giant cells, in the alveolar spaces (Figs 121 and 122).

Conclusion: Pneumonia, predominantly mononuclear.

Case 105

Clinical details: Male aged 4 months. This child was "off colour" one evening; at 0300 hours, 21 October 1957, it was seen by the father, awake but not distressed. Two hours later the mother heard the infant crying, he would not take his feed, but she was not alarmed by the child's condition. Three and a half hours later, at 0830 hours, it appeared to be very ill, with rapid, laboured respirations and "bubbling in its chest" and it died within the next hour.

Autopsy findings: Well nourished. Frothy mucus was seen in the mouth and nostrils and the larynx and trachea contained much thick mucus. The lungs were congested and firm, the lower lobes particularly so, and mucoid material could be expressed from the small bronchi. There were 2 small intestinal intussusceptions deemed to be agonal as there was no accompanying congestion or necrosis.

Opinion: Toxaemia due to acute respiratory infection.

Histological examination: (Sections no longer available for photography). The lungs showed widespread collapse alternating with areas of oedema. The bronchioles showed epithelial desquamation and the alveolar walls were thickened by congestion and an infiltration of polymorphs.

Conclusion: Fulminant pneumococcal pneumonia.

Case 182

Clinical details: Female aged 4½ months. This child had been "irritable" for 2 days, but this had improved and the parents did not think the child ill enough to summon medical assistance. They returned home at 0300 hours, 12 February 1959, to find the infant "frothing at the mouth". The baby-sitter had not heard any noise. A doctor summoned immediately found the child ashen in hue and only one gasping respiration was noticed. It was dead before arrival at hospital.

Autopsy findings: Well nourished, pale. Cerebro-spinal fluid appeared to be in excess, but was clear and normal. Some pleural petechiae, lungs considerably congested with a very small quantity of brownish fluid at the bifurcation of the trachea.

Opinion: Respiratory failure, ? fulminant infection.

Histological examination: (Sections no longer available for photography). The lungs showed congestion with oedema and acute emphysema in areas. The bronchi and bronchioles showed epithelial desquamation and contained gram-positive cocci morphologically resembling staphylococci. Some alveoli contained an exudate with large mononuclear cells, sometimes giant cells. The remaining organs showed nothing of note.

Conclusion: Early mononuclear pneumonia.

Case 63

Clinical details: Male aged 7 months. Slight cough for 2 weeks then suddenly appeared ill one morning, admitted to hospital at 0925 hours, 25 February 1957, with a pyrexia of 103°F, pulse rate 170 per minute, respiratory rate 60, mild cyanosis and numerous rhonchi in the chest. The child was desperately ill and died 5 hours later despite intensive theraphy.

Autopsy findings: Well developed, well nourished. General congestion of all organs, a little mucoid material in trachea, the congested lungs showed scattered patches of broncho-pneumonia consolidation.

Opinion: Acute broncho-pneumonia.

Histology: None available.

Case 206

Clinical details: Male aged 7 months. A medical officer examined this child on the evening of 21 November 1959, it had mild bronchitis with a temperature of 99.6°F. No anxiety was felt. The baby appeared better next day until at 2000 hours the mother noticed it was unresponsive. The medical officer who saw the child half an hour later found it very ill, with cyanosis, temperature 98.6°F, respiratory rate 50 and pulse rate 180 per minute. There were numerous rhonchi and crepitations all over the lung fields and signs of meningism. The infant died a few minutes after admission to hospital at 2045 hours, 22 November 1959.

Autopsy findings: Pericardial petechiae. There was a sero-purulent exudate in the right pleural cavity with fibrinous pleurisy. Both main bronchi showed marked mucosal congestion and pus in the lumen, there was an abscess cavity in the right lower lobe in communication with the right main bronchus.

Opinion: Asphyxia. Rupture of lung abscess into bronchus.

Histological examination: (Slides no longer available for photography). The larger bronchi showed epithelial desquamation, in the smaller ones the epithelium was intact, the peribronchial areas were infiltrated with small round cells and polymorphs. The surrounding lung tissue showed some acute emphysema and thickening of the alveolar walls. There were widespread areas of consolidation and haemorrhage with infiltration of small round cells, large mononuclears and multinucleated cells and polymorphs in the alveolar walls and spaces. The pleura was infiltrated with inflammatory cells. Numerous clumps of gram-positive cocci morphologically resembling a staphylococcus were present in the consolidated areas and the pleura.

Conclusion: Acute staphylococcal pneumonia.

Case 229

Clinical details: Female aged 7 months. This infant became ill suddenly on the afternoon of 1 March 1960, with respiratory signs. She was admitted to hospital at 1645 hours deeply cyanosed and dyspnoeic, and despite energetic treatment including hydrocortisone, adrenalin, chloramphenicol and tracteostomy, she died at 1900 hours, just over 2 hours later.

Autopsy findings: Well nourished. Small haemorrhagic pericardial effusion. Acute inflammation of the trachea and bronchi which contained viscid blood-stained material. The upper and lower lobes of the right lung and the lower lobe of the left showed a uniform haemorrhagic consolidation, the remaining 2 lobes were collapsed.

Opinion: Haemorrhagic pneumonia.

Histological examination: The lungs showed congestion with foci of intra-alveolar haemorrhage. The bronchial epithelium

was mainly intact, their walls were infiltrated with small round cells and polymorphs and their lumen often contained mucus plugs(Fig 123). The alveolar walls were thickened with large and small mononuclear cells and polymorphs. Large mononuclears were seen in the exudate in the alveolar spaces (Fig 124).

Conclusion: Pneumonia, predominantly mononuclear.

Case 39

Clinical details: Female aged 7 weeks. This infant had been treated for an aural discharge by the regimental medical officer, who did not think the illness serious. About 1600 hours, 27 September 1956, the infant developed respiratory distress. She was admitted to hospital cyanosed and collapsed with a temperature of 106°F, pulse rate of 200 per minute and respiratory rate 76. The lungs showed no abnormal physical signs. Despite intensive antibiotic and supparative therapy, the infant died less than 6 hours later.

Autopsy findings: Well developed. Slight discharge from left ear. Examination showed general congestion, but no focal pathological changes were found.

Opinion: No obvious cause of death, ?acute pneumonia and septicaemia.

Histological examination: The lungs were congested with areas of acute emphysema. The bronchial epithelium was intact, the alveolar walls in many areas were thickened and contained small and large mononuclear cells and polymorphs, and some small mononuclear cells were seen in the exudate in alveolar spaces (Figs 125 and 126). Other organs showed congestion.

Conclusion: Interstitial pneumonia.

Serial 4

4. An Infant in whom Autopsy showed signs of Meningitis

Case 28

Clinical details: Male aged 13 months. This child had a slight cold and cough, treated by a medical officer and no serious condition was suspected until it was found at 0330 hours, 26 January 1957, "breathing badly with a rattling sound in the chest". It died a few minutes later.

Autopsy findings: Normal development, some dehydration. Slight cyanosis of extremities. Intense inflammation of meningeal vessels and a gelatinous exudate in the subarachnoid space, with excess cerebro-spinal fluid (Protein 200 mgm/%, Globulin positive, Chlorides 780, Sugar 65, Cells 2250 per cu mm, 10% polymorphs. No pathogen isolated). The brain itself was oedematous. The lungs were not unduly congested, the bronchi contained some mucus and a little vomitus.

Opinion: Meningitis.

Histological examination: (Slides no longer available for photography). The meninges showed gross congestion and oedema; the brain showed no evidence of acute inflammatory change, but some large neurones in the region of the medulla and in the spinal cord showed degenerative changes with nuclear karyorrhexis or loss. There was no glial reaction nor neuronophagia.

Conclusion: Acute encephalo-meningitis.

Serial 5A

5. Infants in whom Autopsy showed Congenital conditions of a Major Nature

Case 65

Clinical details: Male aged 5 weeks. This infant was found to have a congenital abnormality of the heart on post-mortem examination, but appeared to be thriving. He was attended to

by the mother at 2330 hours, and appeared to be all right, he was found dead at 0545 hours, 13 March 1957.

Autopsy findings: Well nourished. Cyanosis of extremities. Bilateral cataract. The organs showed general congestion. There were petechiae of the pleurae and pericardium. The respiratory tree was congested and contained mucus. The heart was grossly enlarged (56g in weight), the ductus arteriosus was patent, as large as the pulmonary artery and the foramen ovale was patent. The liver was large, the spleen large and firm.

Opinion: Cardio-respiratory failure from congenital cardiac defects.

Histology: None available.

Serial 5B

B. Cases with Previous Mild Symptoms

Case 67

Clinical details: Female aged 9 months. This infant had been diagnosed as a mongol. There had been past episodes of respiratory disease, but the child had been apparently well for some time, then developed a cold and was found dead on the morning of 19 March 1957.

Autopsy findings: Reasonably well nourished infant, not markedly mongoloid in appearance. The lungs showed patchy consolidation, the heart was grossly enlarged, especially the right side and there was a large defect in the upper half of the intraventricular septum.

Opinion: Broncho-pneumonia accompanied by congenital cardiac defect.

Histological examination: The lungs showed widespread consolidation, in areas this was broncho-pneumonia in type, with partial disruption of bronchioles and infiltration of

inflammatory cells, polymorphs predominating (Figs 127 and 128); in other areas the consolidation was predominantly due to large and small mononuclear cells in the alveoli (Fig 129).

Conclusion: Acute pneumonia, broncho-pneumonic in type.

Case 202

Clinical details: Male aged 21 months. Was seen at a clinic 2 days before death with a severe rhinitis, the chest however showed no abnormal physical signs and the infant was apyrexial. Found dead on 29 October 1959.

Autopsy findings: The head was large, there was a bilateral genu varum. The vault of the skull was large, the skull bones thin and the ventricular system of the brain distended. The aqueduct of Sylvius was patent. The cerebral sulci were very shallow. There was a bilateral pleural effusion (400 ml) with mucopurulent material in the trachea and bronchi and consolidation of the red hepatization type in the lower lobes of both lungs and in the right middle lobe.

Opinion: Pneumonia in a hydrocephalic infant.

Histology: None available.

Serial 5C

C. A Case Dying in the Presence of Adults

Case 19

Clinical details: Male aged 11 months. This infant had a bilateral inguinal hernia and phimosis. Operation was arranged for January 1956, but postponed until May as the child had developed bronchitis. At operation it collapsed as the prepuce was incised and resuscitation was of no avail.

Autopsy findings: Well developed, plump infant. The anterior fontanelle was 3cm in diameter. The brain was congested, with eodema over the vertex, the cerebro-spinal fluid was clear but excessive in amount and there was a firm,

flat oval tumour, 3 x 2.5 x 1.3 cm in the region of the posterior horn of the right lateral ventricle. The heart was hypertrophied but otherwise no cardiac abnormality was found. The walls of the respiratory tree were congested and the lumen contained mucoid material.

Opinion: Death from cerebral anoxia during operation in an infant with increased intracranial pressure due to a tumour of the left parietal region.

Histological examination: The trachea and main bronchi showed some epithelial desquamation and a marked infiltration of the underlying tissue with small round cells, polymorphs and macrophages (Fig 130). The lungs were congested, with areas of oedema and some acute emphysema, the alveolar walls were thickened with small round cells and congestion, the lumen of the alveoli contained large mononuclear cells (Fig 131). The main cells seen in the alveolar spaces were these large mononuclears and there was a suggestion of hyaline membrane formation in some (Fig 132). The brain lesion described consisted of brain tissue with a number of abnormal gemistocytic cells, binucleated or tri-nucleated and other large abnormal astrocytes which showed a cytoplasmic component. All the organs showed congestion.

Conclusion: The lungs show a severe tracheo-bronchitis and mononuclear pneumonia. The brain lesion is interpreted as being an astrocytoma or some obscure congenital defect, opinion favours the latter diagnosis.

Serial 6

Case 244

6. An Infant in whom Autopsy showed Emaciation only

(No history of serious illness)

Clinical details: Male aged 6 weeks. This infant was discharged from hospital on 19 April 1960, apparently thriving since birth one week before. According to the parents there had been no serious illness but the child was lethargic one morning and on admission to hospital on 24 May, 1960, it was moribund, emaciated and somewhat dehydrated, with peripheral cyanosis and spasmodic respirations which ceased half-an-hour later. Lumbar puncture revealed a normal cerebro-spinal fluid.

Autopsy findings: An emaciated infant with leathery skin and no subcutaneous fat. Examination revealed no pathological change in any of the organs.

Opinion: Inanition due to emaciation.

Histology: None available.

Serial 7

Case 242

7. Infants Dying from Accidental Causes

Clinical details: Female aged 18 months. Found dead in a brook near her home at 1145 hours, 6 May 1960. Artificial respiration was of no avail; much water drained from the lungs.

Autopsy findings: Well nourished. The respiratory tree contained blood-stained frothy fluid, the lungs were very oedematous and frothy blood-stained fluid was expressed from the cut surfaces, but not copiously. The stomach also contained water.

Opinion: Death from drowning.

Histology: None available.

Case 183 | Clinical details: Male aged 23 months. Electrocuted with a broken electric iron at 0815 hours, 14 July 1959.

Autopsy findings: Burn marks on inner aspect of thumbs and middle fingers of the right hand. The trachea contained a little frothy mucus, the lungs were moderately congested.

Opinion: Consistent with death from electrocution.

Histology: None available.

Case 47 | Clinical details: Male aged one year. This infant was walking with his grandmother in a barrack area on 13 November 1956, when a round from the gun of an armoured car struck a steel door and portions of the missile hit the child who died rapidly before transfer to hospital.

Autopsy findings: Penetrating wounds of chest and abdomen damaging the lungs, liver (the latter being pulped) and the kidneys.

Opinion: Multiple injuries from shell fragments.

Histology: None available

Case 22 | Clinical details: Female aged one year. This infant fell out of the third-floor window at 2015 hours, 30 May 1956. Unconsciousness gradually deepened and she died at 0345 hours next morning.

Autopsy findings: Comminuted fractures of vault of skull and fracture of base with widespread haemorrhage and brain contusion.

Opinion: Cerebral injury due to trauma.

Histology: None available.

Case 37 | Clinical details: Male aged 3 weeks. This infant was given a sweet by a 3 year old boy, it choked and was found dead on 19 September 1956.

Autopsy findings: Normal development. Intense cyanosis of upper part of body and extremities. General congestion throughout, including respiratory tree and lungs, the cut surface of the latter oozed blood stained watery fluid. The pericardium showed petechiae. Nothing was found obstructing the respiratory passages.

Opinion: Asphyxia; findings consistent with history of choking on a sweet.

Histology: None available.

Case 44

Clinical details: Female aged 11 months. This infant was found dead at 1245 hours, 22 October 1956, with the cord of an electric light switch beside its cot round its neck, causing an indented mark.

Autopsy findings: A circular 0.3 cm mark round neck at level of thyroid cartigage. About this mark there were numerous skin petechiae. The tongue was blue and protruded from between the teeth, the eyes were protruberant. There were haematomata at the bifurcation of the common carotid arteries, pericardial petechiae and a distended right ventricle of the heart. The main bronchi contained a little mucus and the congested lungs had some pale emphysematous areas.

Opinion: Asphyxia from accidental strangulation.

Histology: None available.

Case 5

Clinical details: Female aged 8 months. This infant was heard crying at 0715 hours, 3 February 1956, and was found at 0730 hours in the corner of her pram with the pram straps twisted round her neck.

Autopsy findings: Marked cyanosis of the upper part of the

body but no evidence of external trauma except for an abrasion over the left shoulder. Multiple cerebral petechiae. The respiratory tree appeared normal, the lungs were congested and the pleurae and pericardium showed petechial haemorrhages. Other organs were congested.

Opinion: Asphyxia. No precipitating cause found, but consistent with the history of strangulation by broad pram straps.

Histological examination: The lungs showed congestion with acute emphysema and desquamation of bronchial epithelium (Fig 133). In the non-emphysematous alveoli there was some thickening of the alveolar walls and small round cells and a few polymorphs were seen, with occasional mononuclear cells lying in exudate in the alveolar spaces (Fig 134).

Conclusion: Terminal changes of a mild inflammatory nature.

Serial 8

Case 213

8. An Infant in whom no Apparent Cause of Death was found at Autopsy (no previous symptoms)

Clinical details: Male aged 4 months. This infant was found dead in the morning of 1 January 1960, no previous history of illness.

Autopsy findings: Well nourished. Some congestion of the lungs and a little greenish mucus in both main bronchi, otherwise nothing of note.

Opinion: Cause of death not apparent.

Histological examination: The brain showed a slight exudate with scattered mononuclear cells and polymorphs in the meninges (Fig 135). The myocardium showed hyaline change with occasional polymorphs between the fibrils (Fig 136). The lungs were congested, with areas of acute emphysema and there were

small areas of consolidation with thickening of alveolar walls and an infiltration of small round cells, large mononuclears, some giant cells and occasional polymorphs in the alveolar walls and spaces (Fig 137). The congested spleen showed prominent follicles with reactive centres.

Conclusion: The minor reactive changes in the meninges, heart and spleen and the pulmonary changes suggest an acute infective condition, probably a fulminant type of septicaemia.

APPENDIX D

ILLUSTRATIVE MICROPHOTOGRAPHS

Note: 1. All sections stained by haematoxylin and eosin

2. Figures in parentheses indicate case number in Appendices A - C.

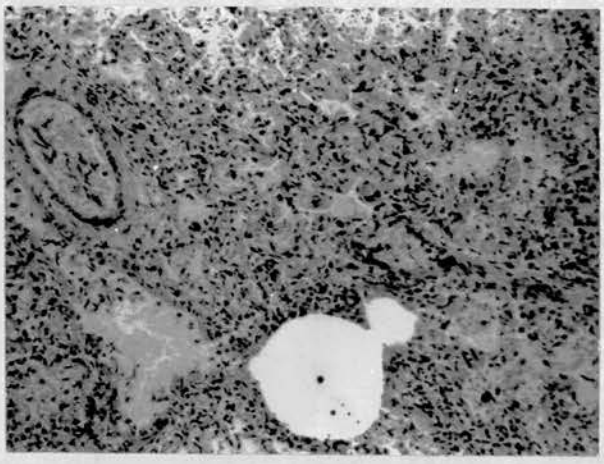

Fig 1(250) Lung x 250
Consolidation

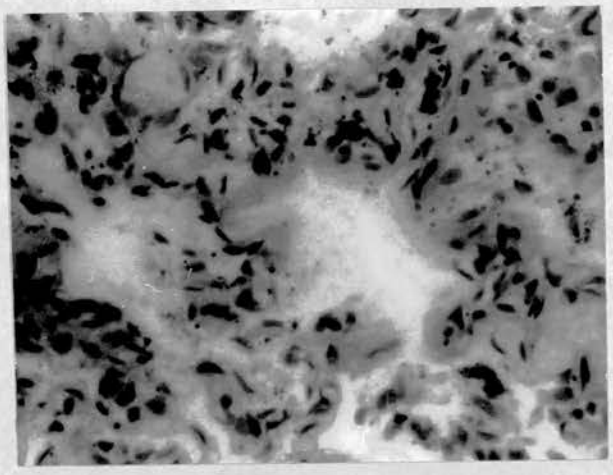

Fig 2 (250) Lung x 1000
Hyaline membrane

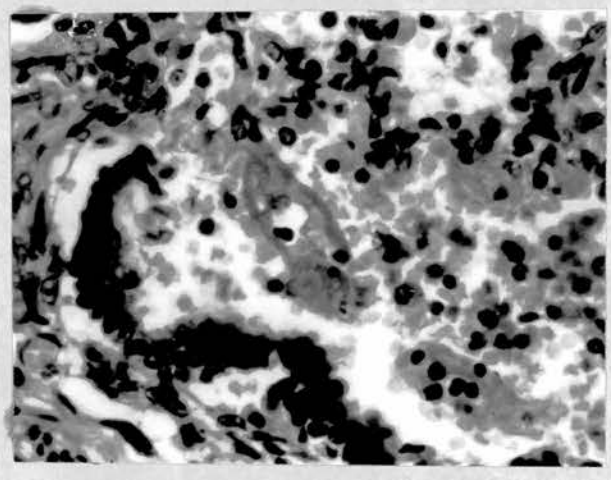

Fig 3 (106) Lung x 1000
Bronchial disruption

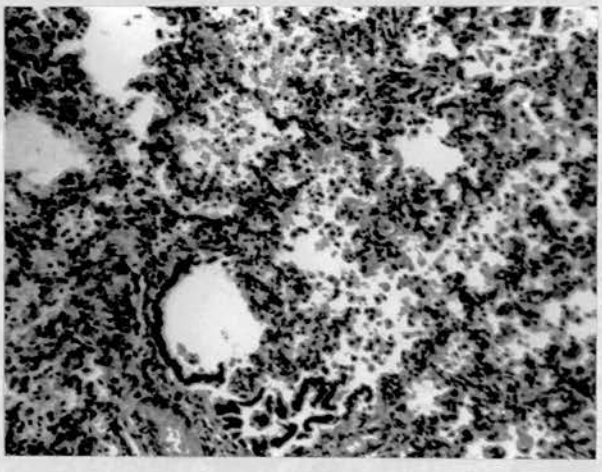

Fig 4 (106) Lung x 250
Monunuclear pneumonia

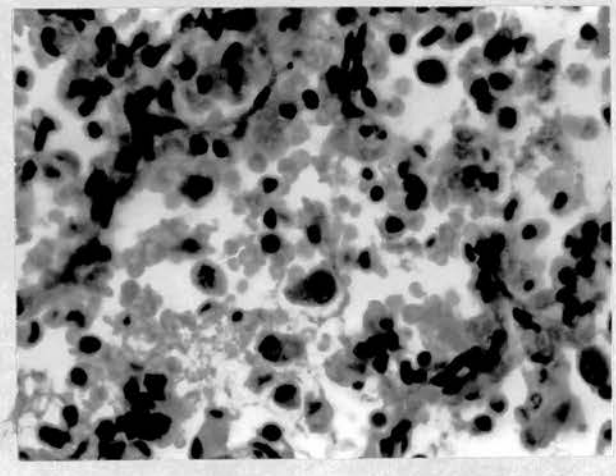

Fig 5 (106) Lung x 1000
Mononuclear pneumonia

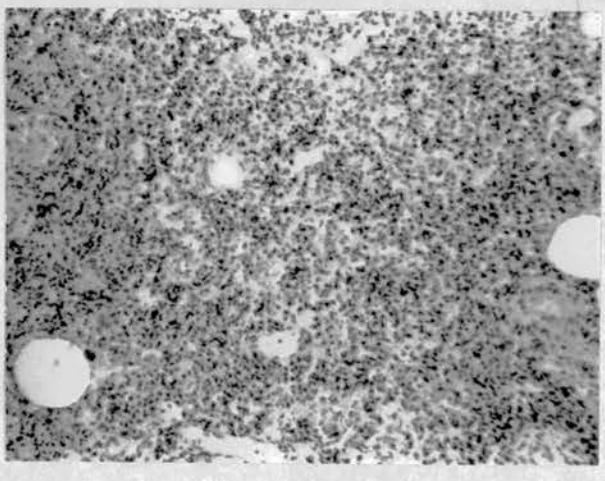

Fig 6 (205) Lung x 250
Consolidation

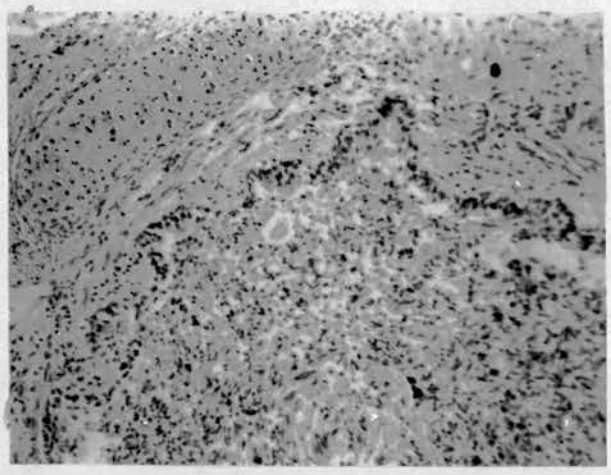

Fig 7 (205) Lung x 250
Disrupted, infected
bronchus

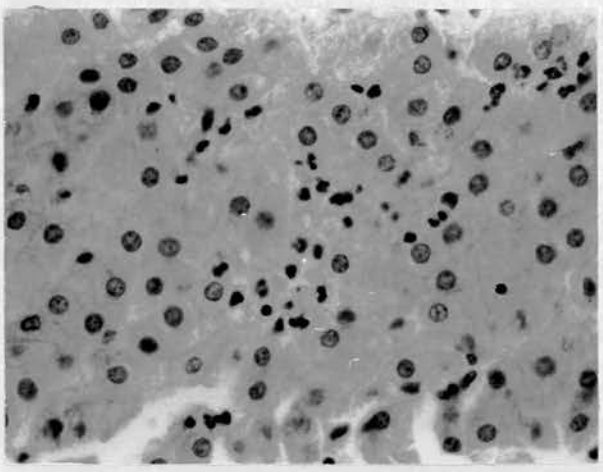

Fig 8 (205) Liver x 1000
Foci of polymorphs

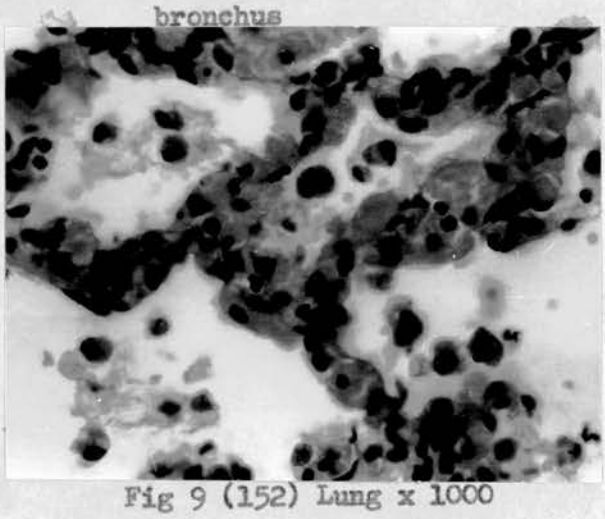

Fig 9 (152) Lung x 1000
Congested; mononuclear
cells.

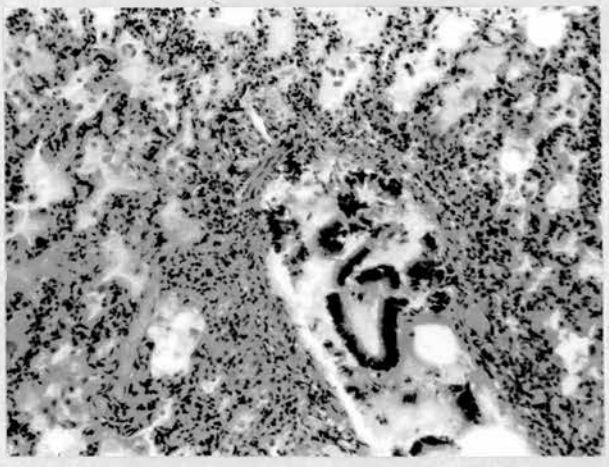

Fig 10 (75) Lung x 250
Mononuclear pneumonia

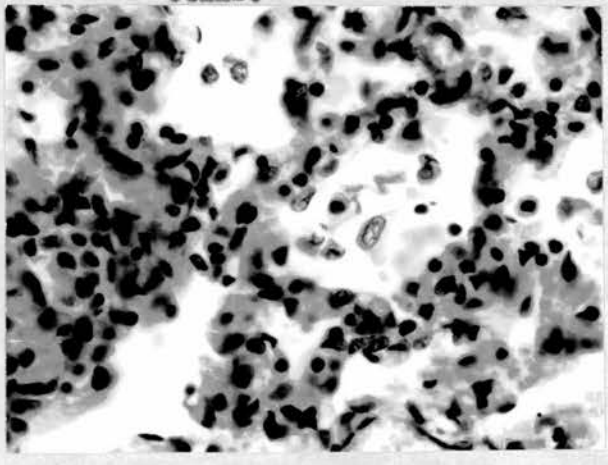

Fig 11 (75) Lung x 1000
Mononuclear pneumonia

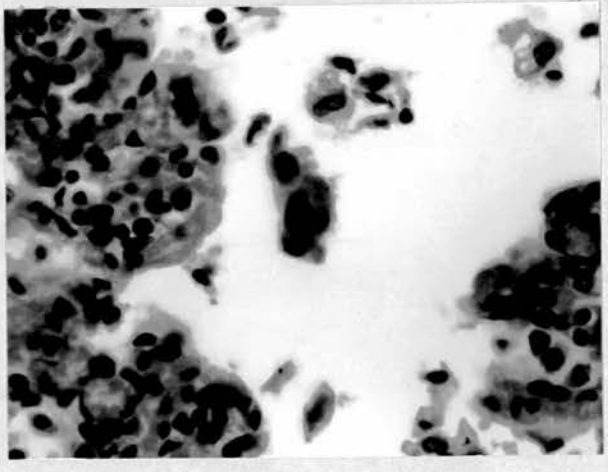

Fig 12 (75) Lung x 1000
Giant cells

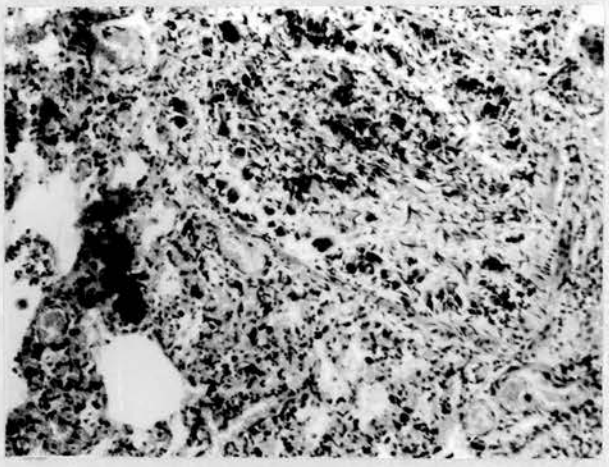

Fig 13 (251) Lung x 250

Desquamated bronchus

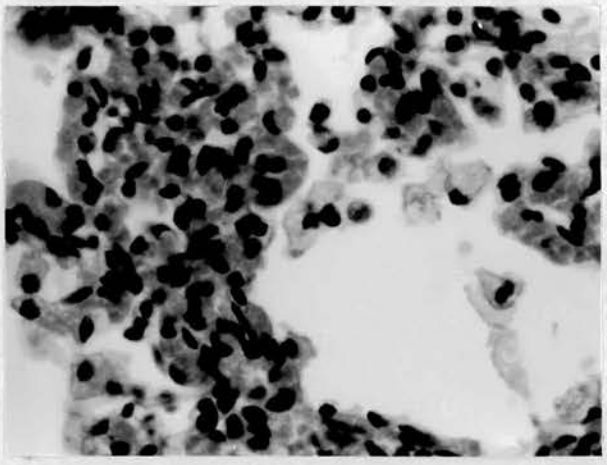

Fig 14 (251) Lung x 1000

Mononuclears and polymorphs

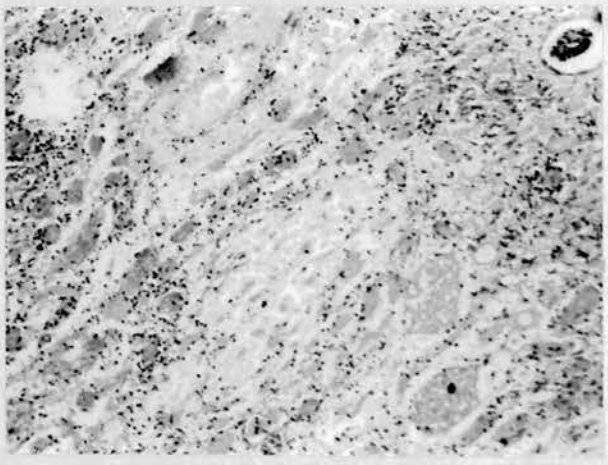

Fig 15 (251) Kidney x 250

Necrosis and infection

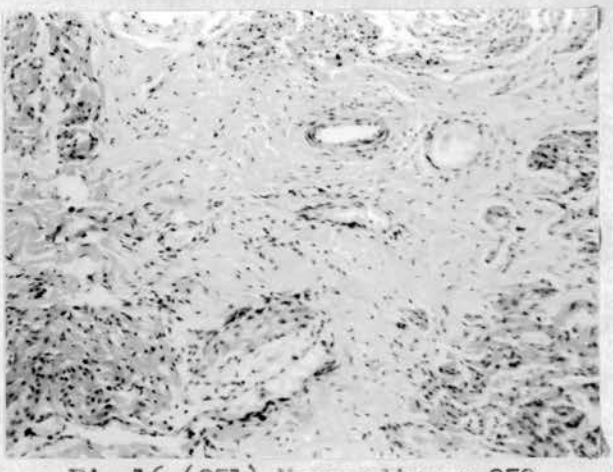

Fig 16 (251) Myocardium x 250

Fibrosis

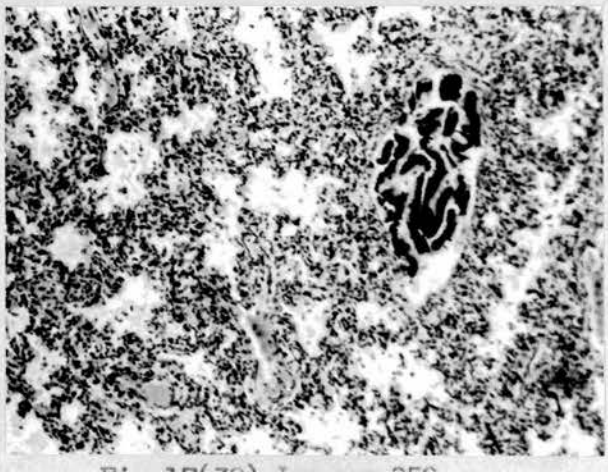

Fig 17(30) Lung x 250

Interstitial pneumonia

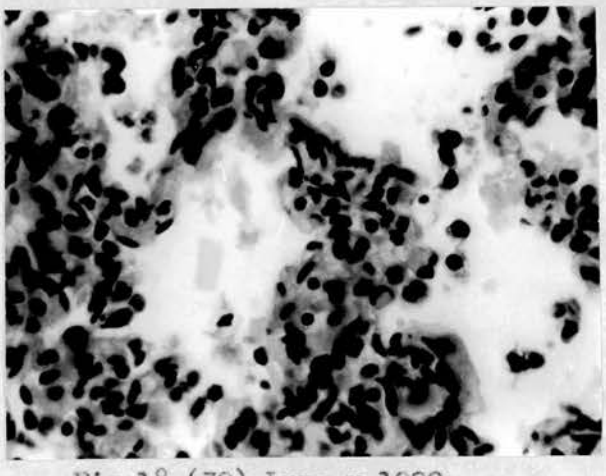

Fig 18 (30) Lung x 1000

Interstitial pneumonia

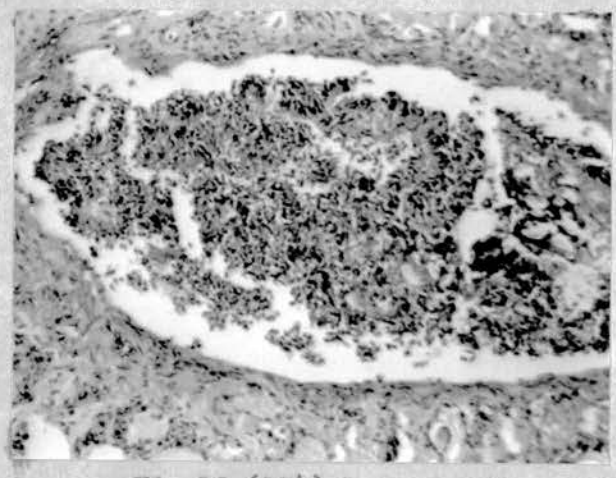

Fig 19 (174) Lung x 250
Desquamated bronchus

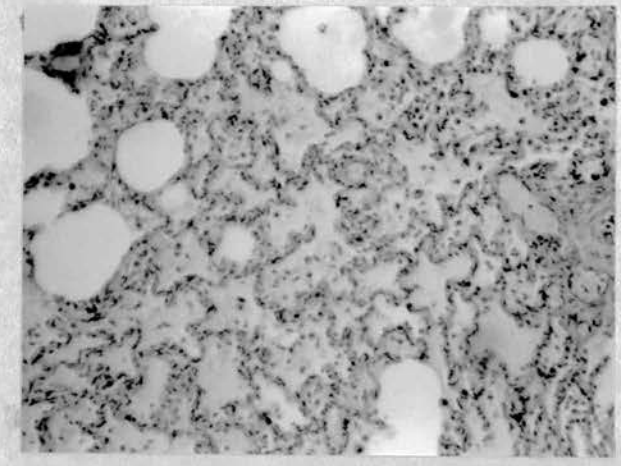

Fig 20 (174) Lung x 250
Mononuclear pneumonia

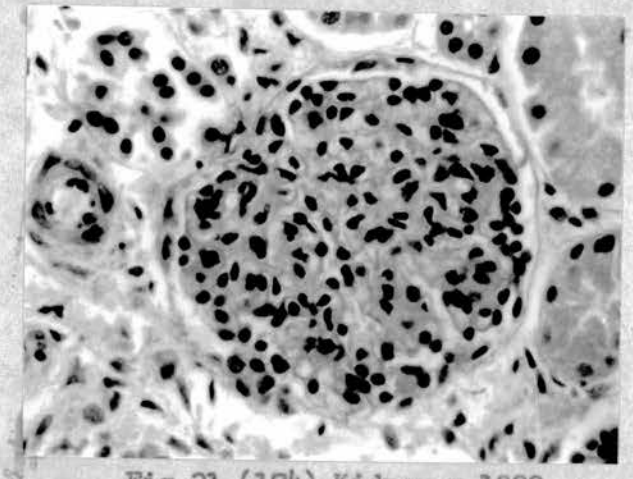

Fig 21 (174) Kidney x 1000
Swollen glomerulus

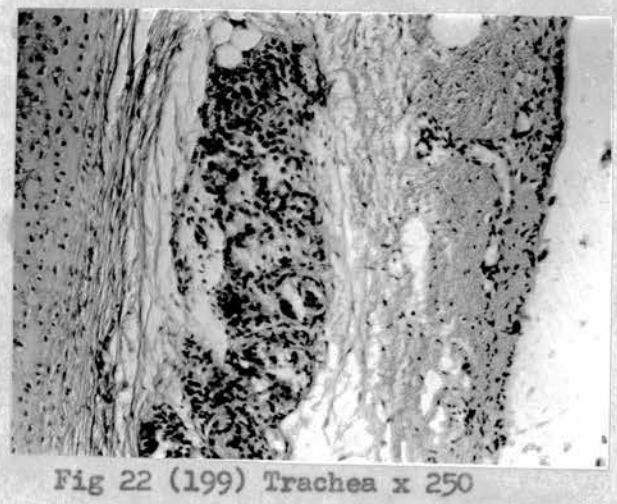

Fig 22 (199) Trachea x 250
Epithelial loss, haemorrhage,
small round cells

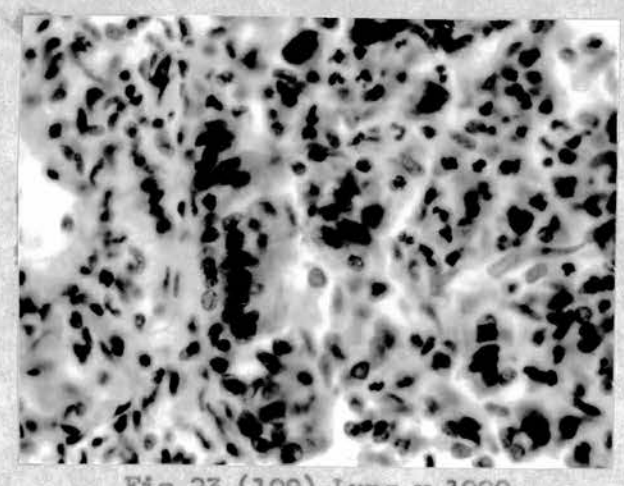

Fig 23 (199) Lung x 1000
Bronchial desquamation
Polymorphs

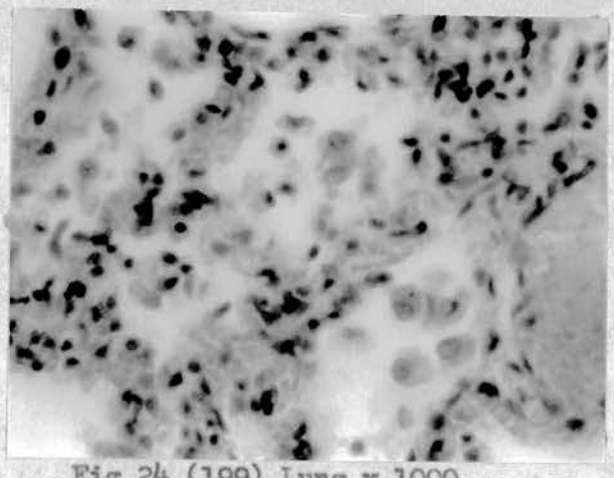

Fig 24 (199) Lung x 1000
Mononuclear pneumonia

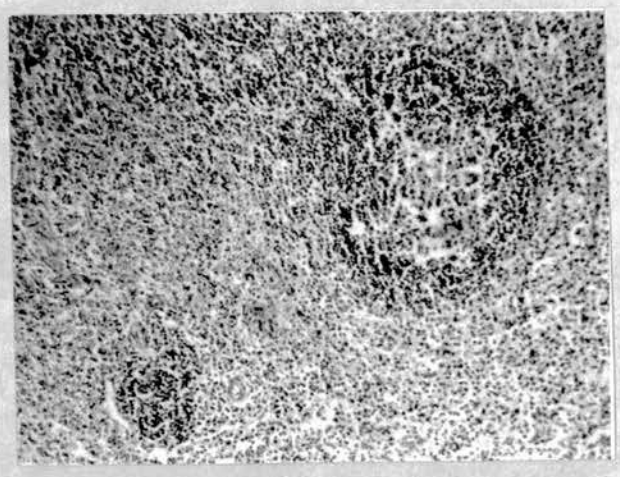

Fig 25(199) Spleen x 250
Reactive changes

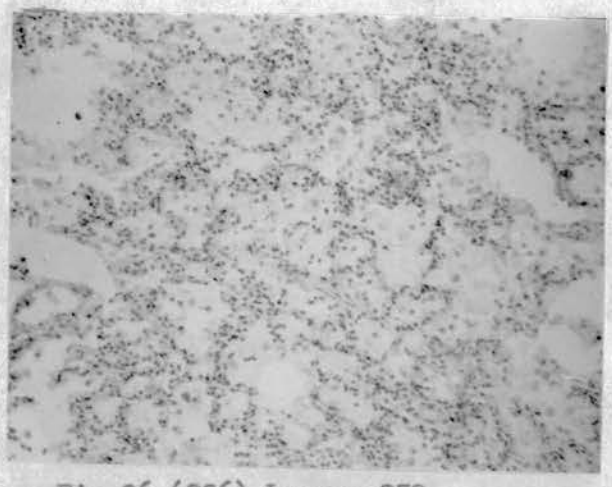

Fig 26 (226) Lung x 250
Mononuclear pneumonia

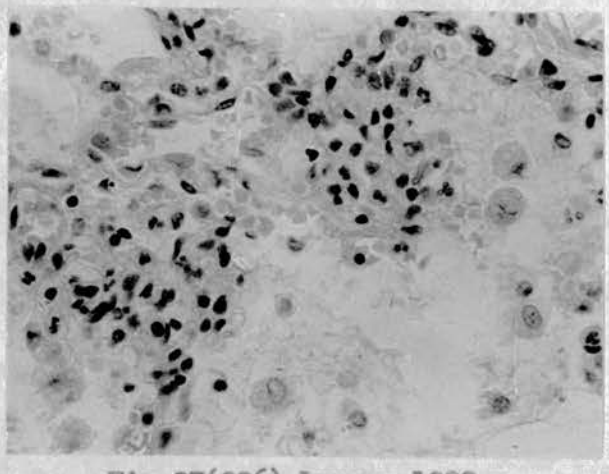

Fig 27(226) Lung x 1000
Mononuclear pneumonia
Some polymorphs

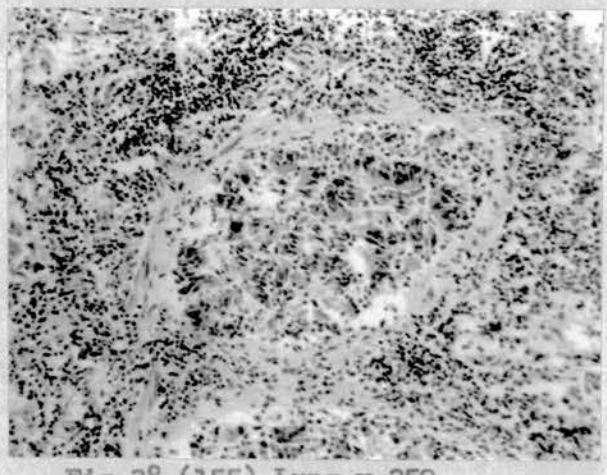

Fig 28 (155) Lung x 250
Desquamated bronchus
Surrounding infiltration

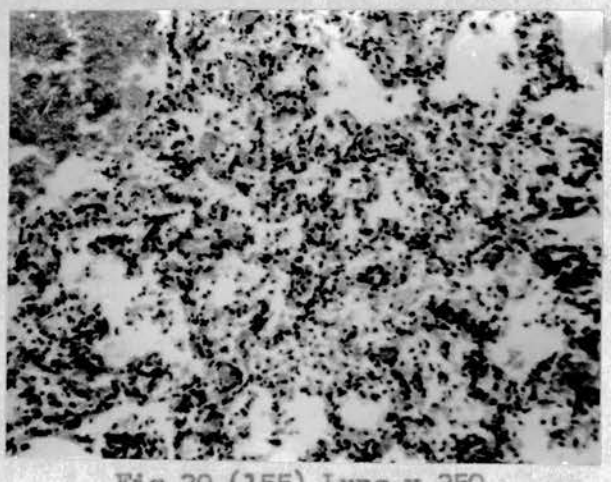

Fig 29 (155) Lung x 250
Mononuclear pneumonia
Area of haemorrhage

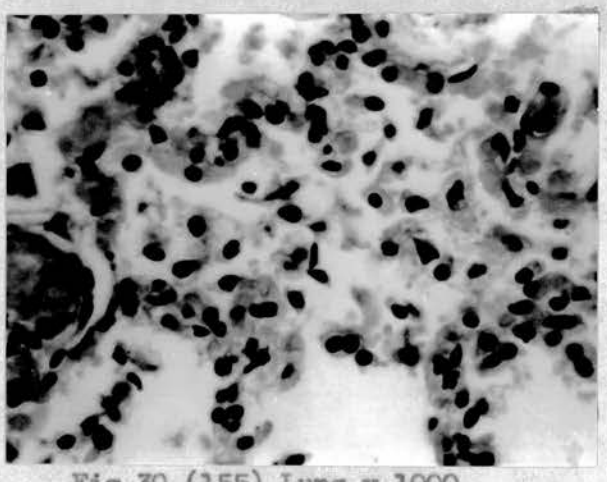

Fig 30 (155) Lung x 1000
Mononuclear pneumonia

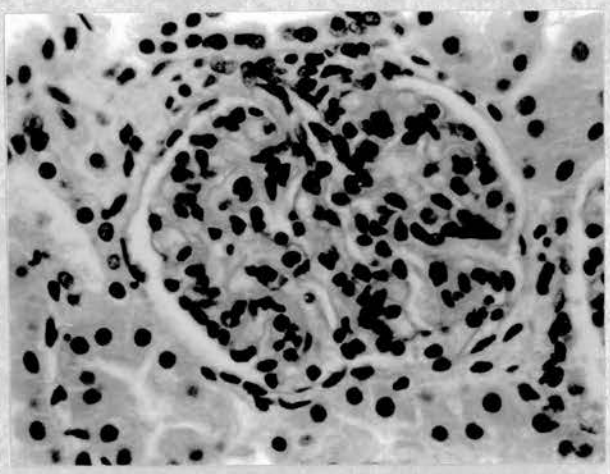

Fig 31 (155) Kidney x 1000
Swollen glomerulus

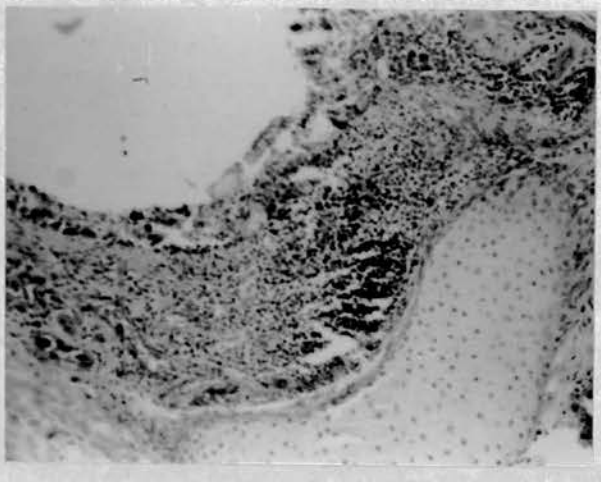

Fig 32 (139) Lung x 250
Infiltrated bronchus

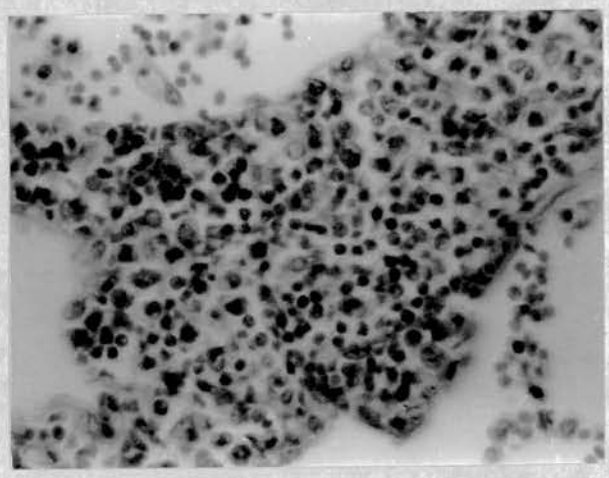

Fig 33 (139) Lung x 1000
Interstitial pneumonia

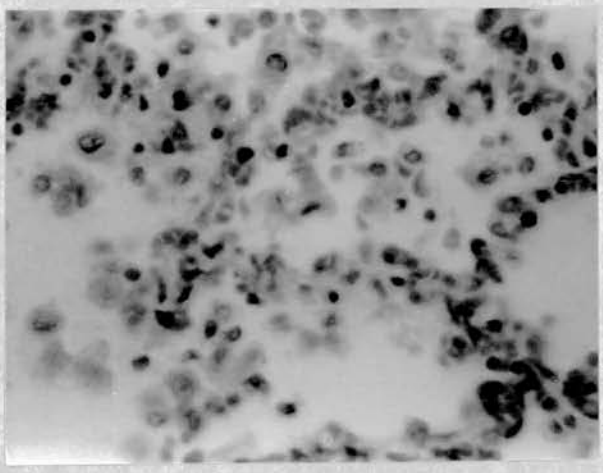

Fig 34 (139) Lung x 1000
Mononuclear pneumonia

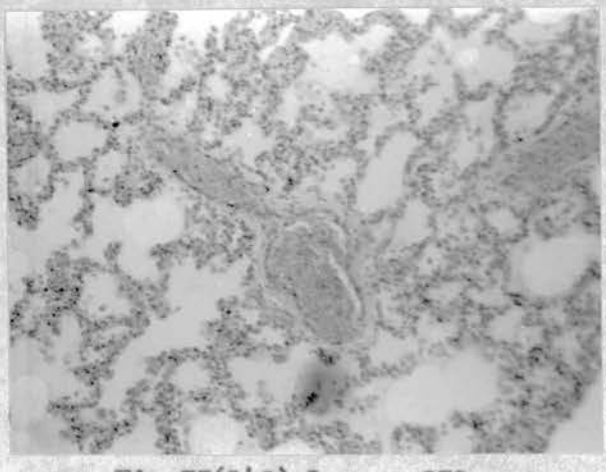

Fig 35(140) Lung x 250
Exudate
Scanty mononuclears

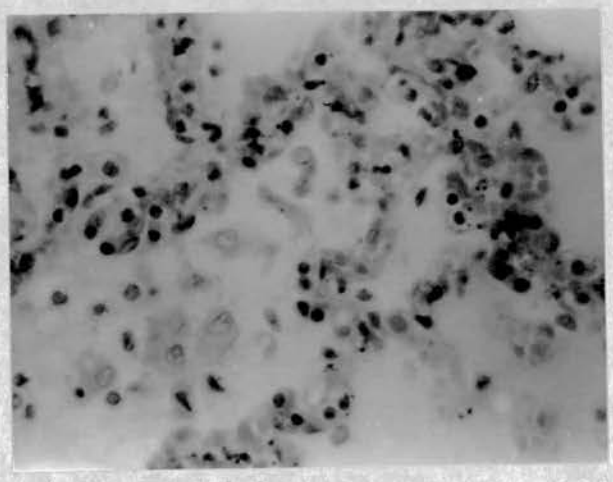

Fig 36 (140) Lung x 1000
Exudate
Mononuclears

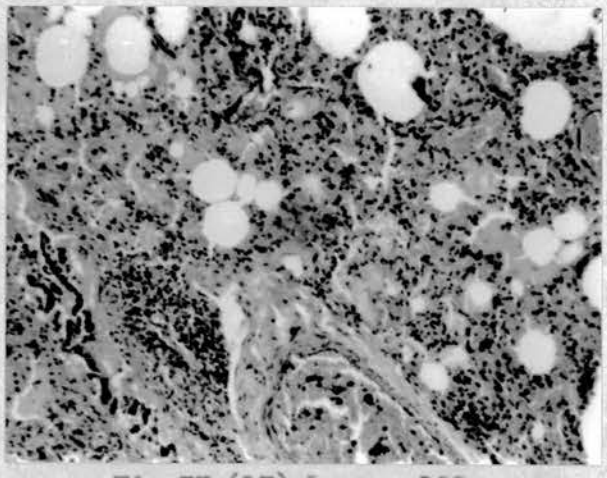

Fig 37 (17) Lung x 100

Consolidation

Disrupted bronchus

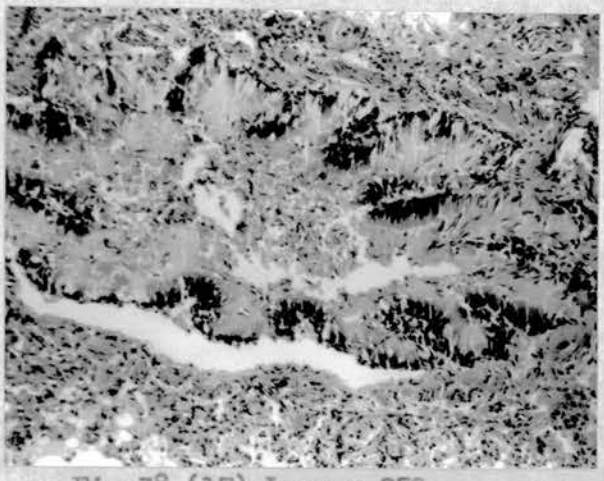

Fig 38 (17) Lung x 250

Disrupted bronchus

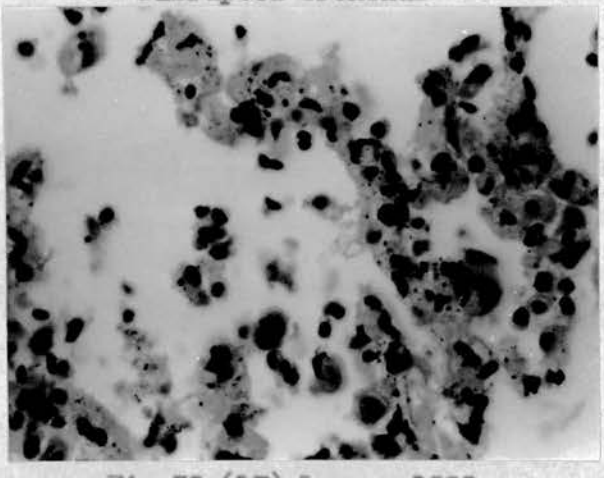

Fig 39 (17) Lung x 1000

Interstitial pneumonia

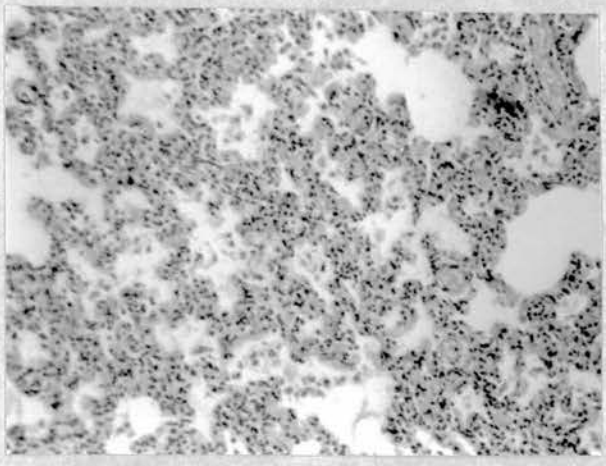

Fig 40 (1) Lung x 250

Mononuclear pneumonia

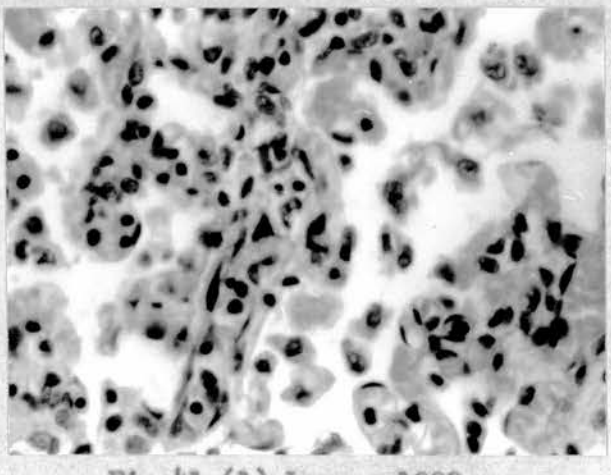

Fig 41 (1) Lung x 1000

Mononuclear pneumonia

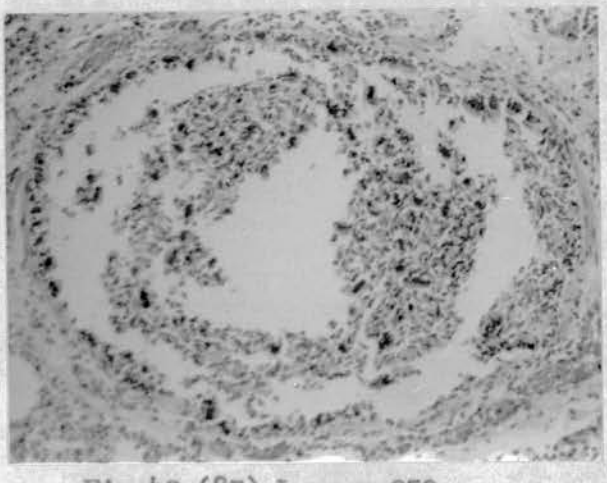

Fig 42 (83) Lung x 250

Desquamated bronchus

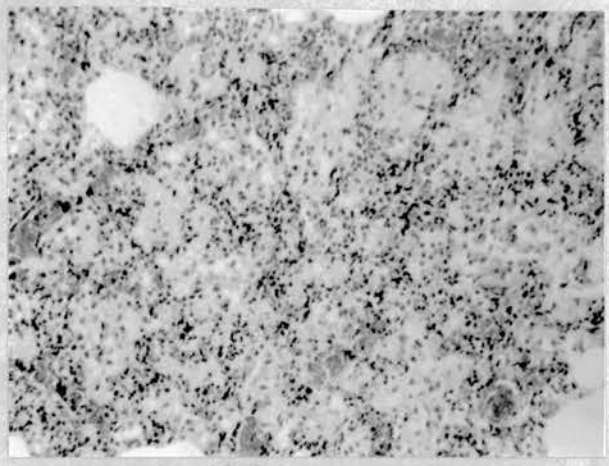

Fig 43 (83) Lung x 250

Mononuclear pneumonia

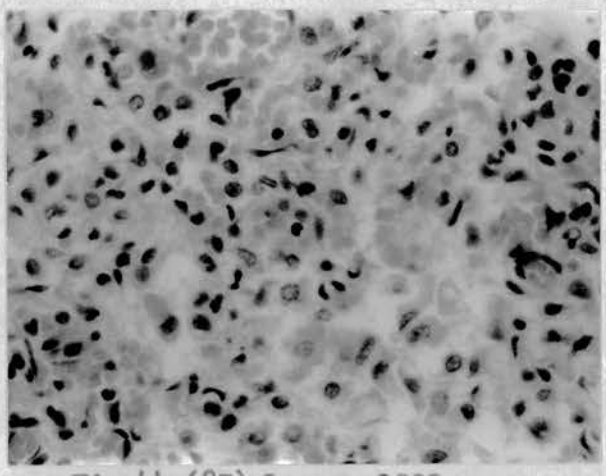

Fig 44 (83) Lung x 1000

Mononuclears and polymorphs

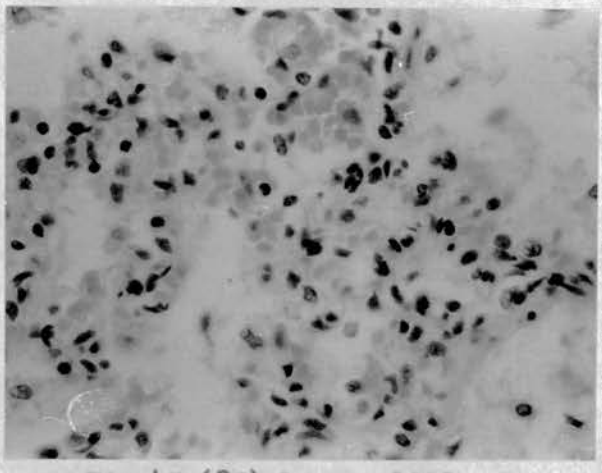

Fig 45 (83) Lung x 1000

Small round cells

Polymorphs

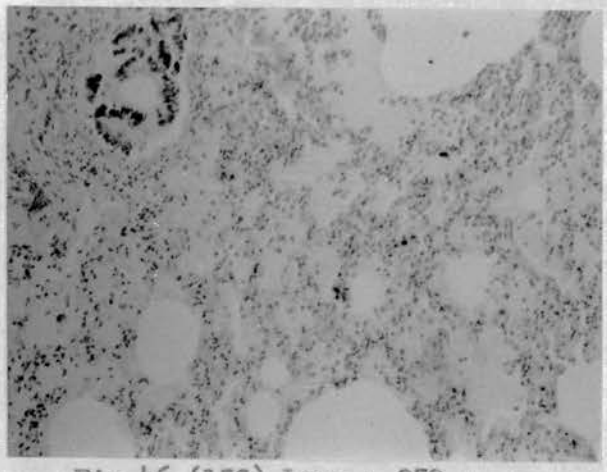

Fig 46 (159) Lung x 250

Mononuclear pneumonia

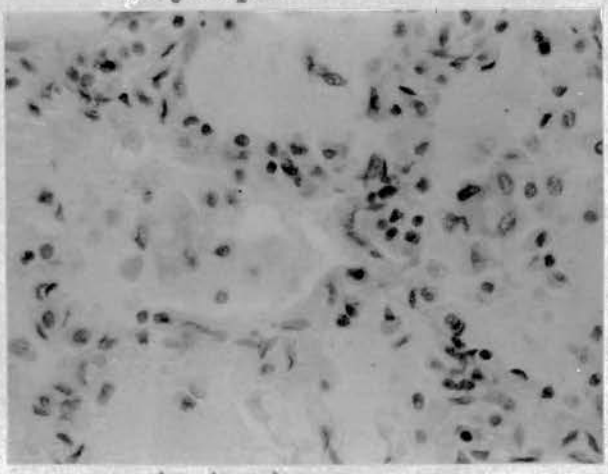

Fig 47 (159) Lung x 1000

Mononuclears

Interstitial polymorphs

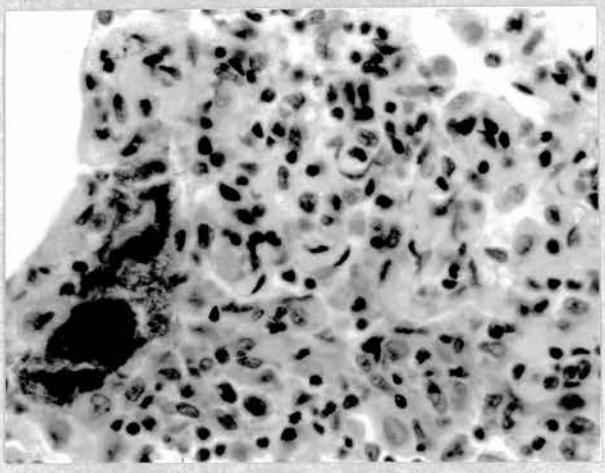

Fig 48(59) Lung x 1000

Infiltration bronchial

wall. Bacterial clumps

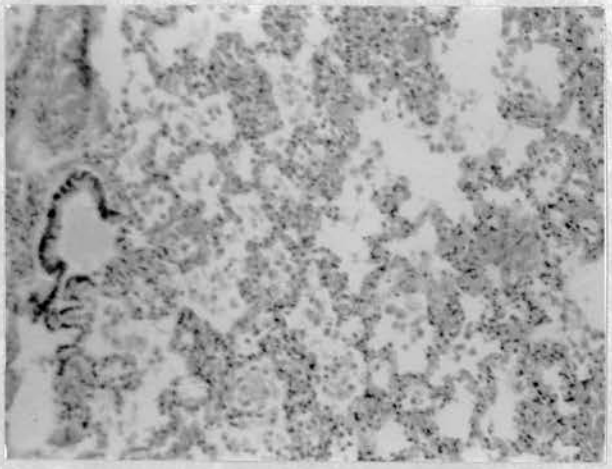

Fig 49 (59) Lung x 250
Mononuclear pneumonia

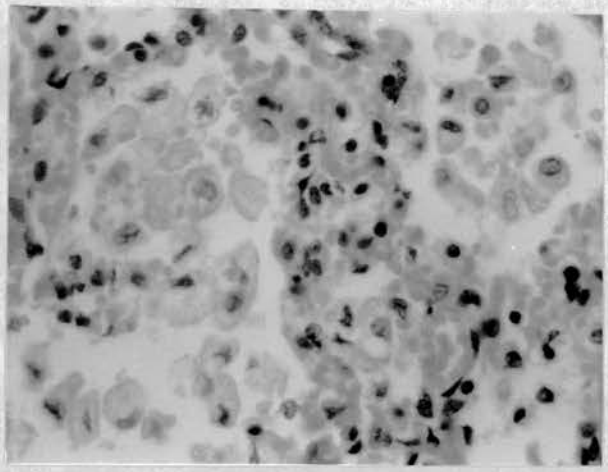

Fig 50 (59) Lung x 1000
Mononuclear pneumonia

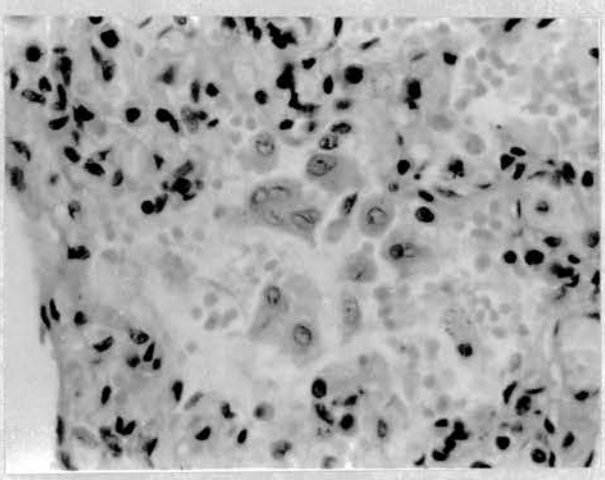

Fig 51 (59) Lung x 1000
Giant cells

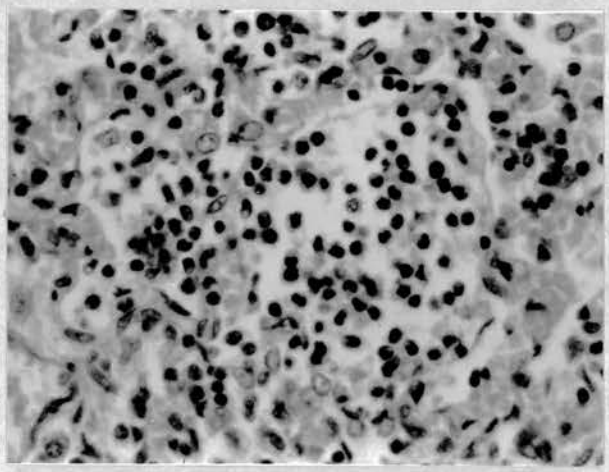

Fig 52 (59) Lung x 1000
Polymorph infiltration

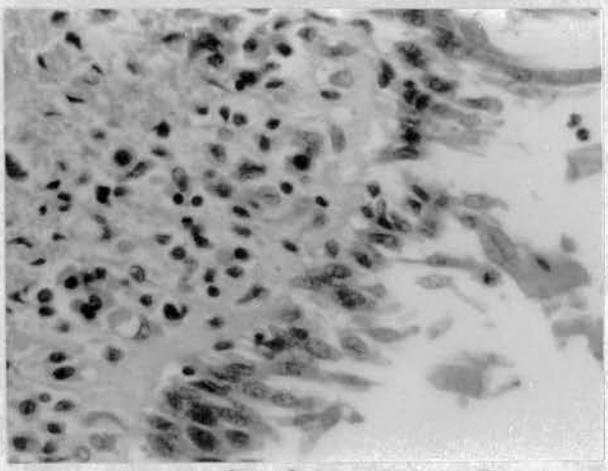

Fig 53 (120) Trachea x 1000
Desquamation
Infiltration

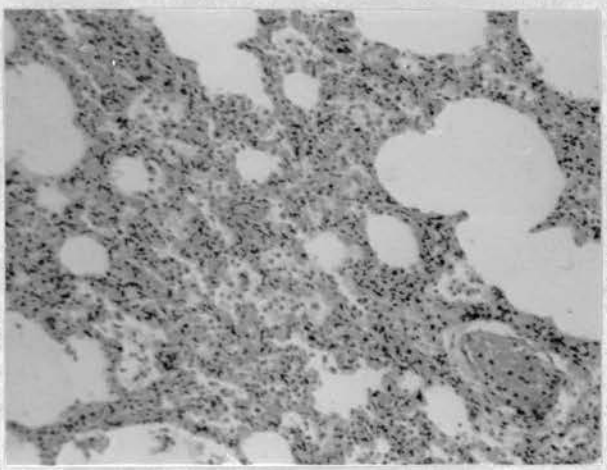

Fig 54 (120) Lung x 250
Mononuclear pneumonia
Emphysema

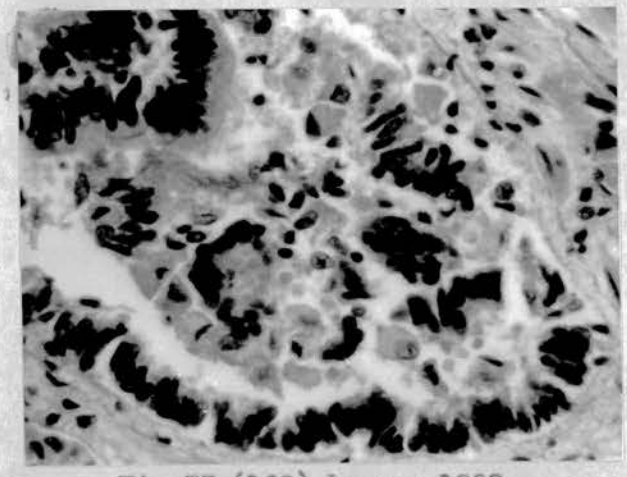

Fig 55 (120) Lung x 1000

Desquamated bronchus

Mononuclears

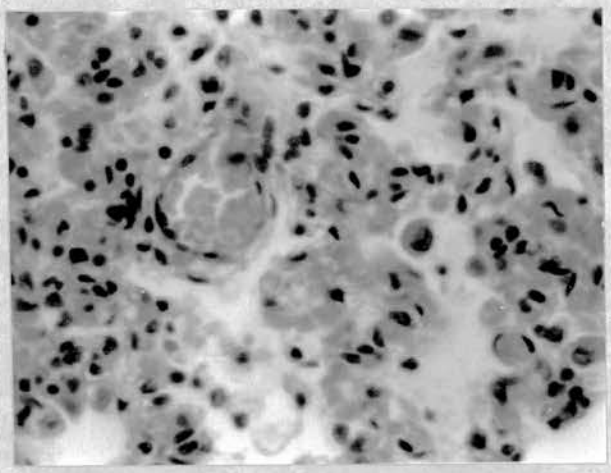

Fig 56 (120) Lung x 1000

Mononuclears and polymorphs

Marked congestion

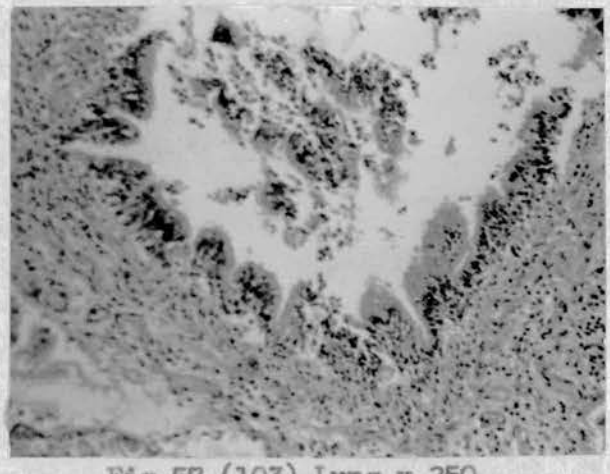

Fig 57 (103) Lung x 250

Desquamated bronchus

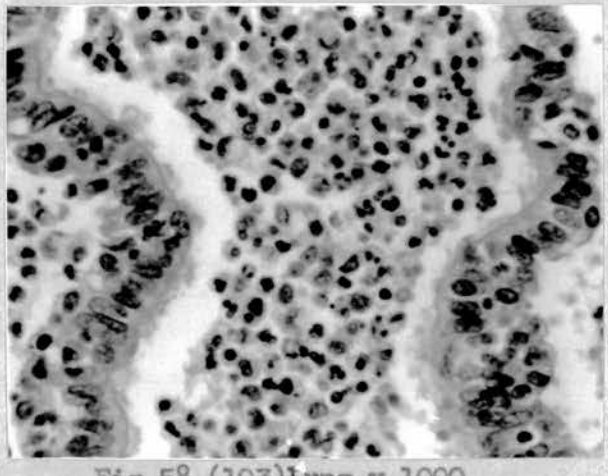

Fig 58 (103) Lung x 1000

Pus in bronchus

Fig 59 (103) Lung x 250

Disrupted bronchus

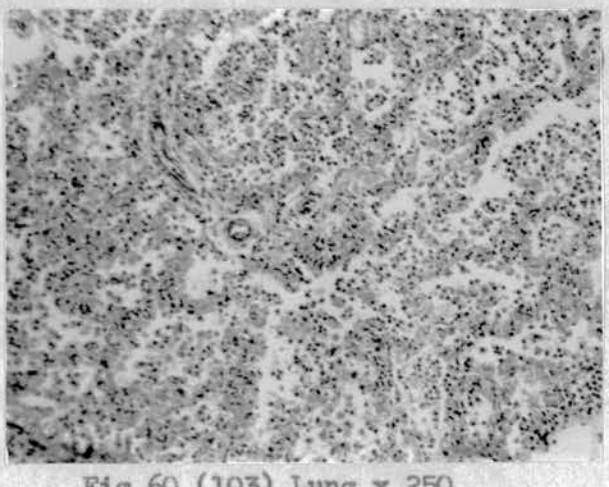

Fig 60 (103) Lung x 250

Mainly mononuclear area

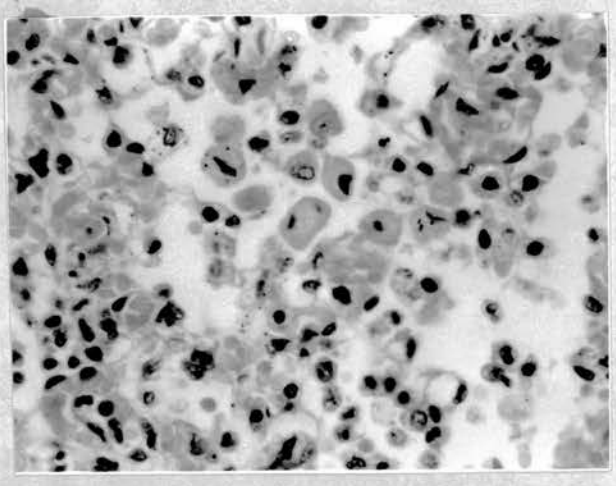

Fig 61 (103) Lung x 1000
Mononuclear infiltration

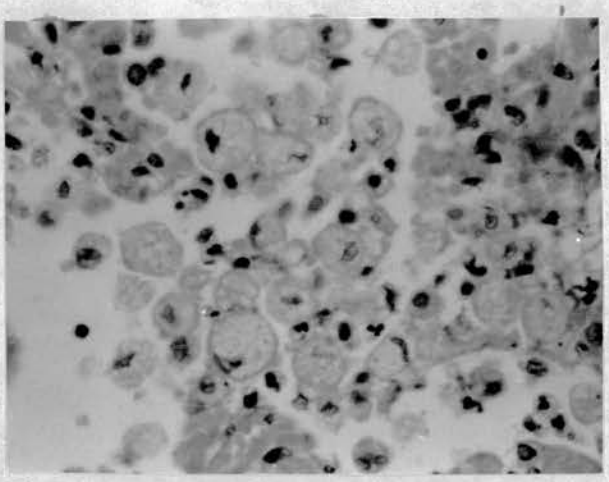

Fig 62 (103) Lung x 1000
Foamy macrophages

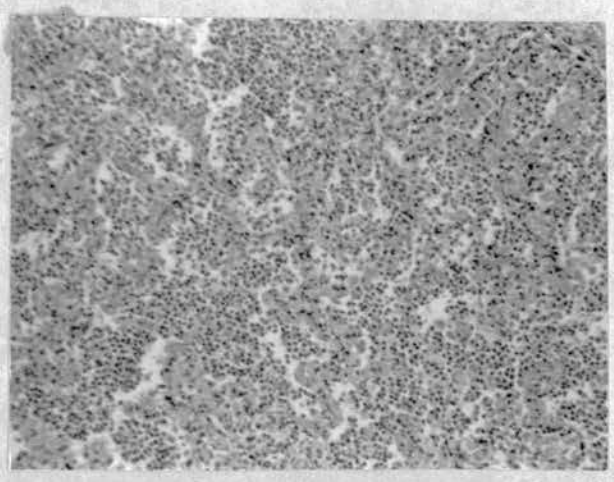

Fig 63 (103) Lung x 250
Frank broncho-pneumonia

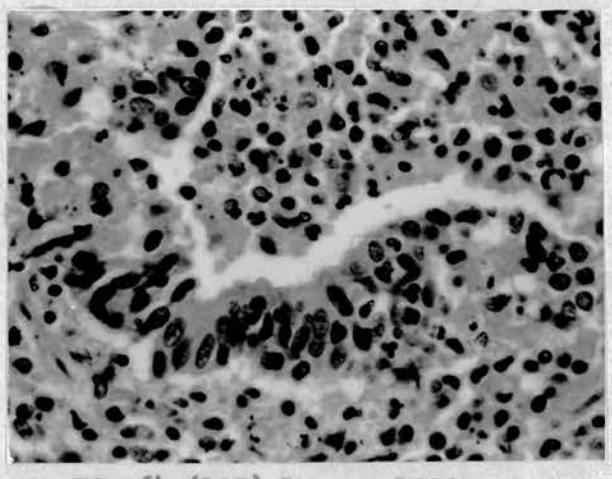

Fig 64 (103) Lung x 1000
Polymorph infiltration

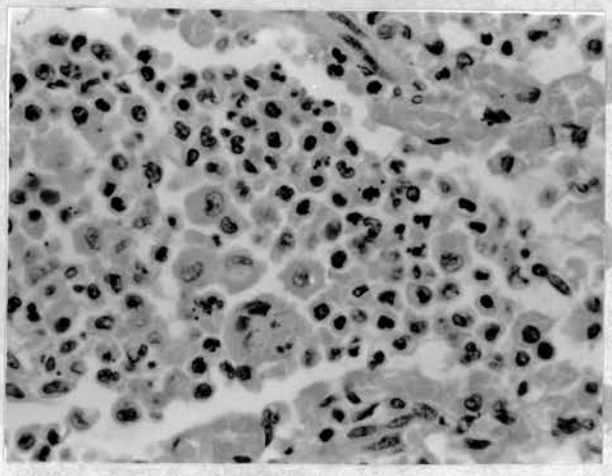

Fig 65 (103) Lung x 1000
Mononuclear and giant cells
Polymorphs

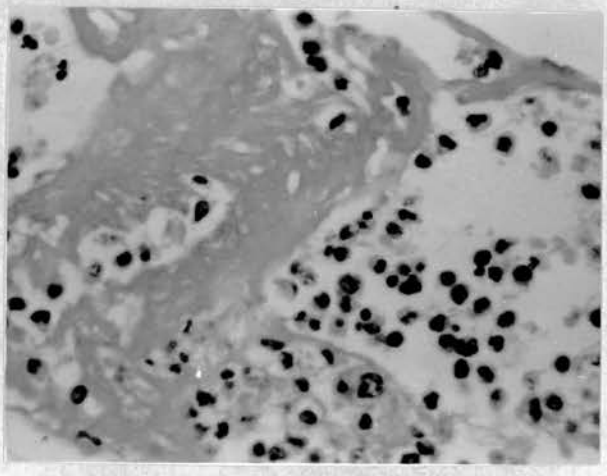

Fig 66 (103) Pleura x 1000
Fibrinous pleurisy

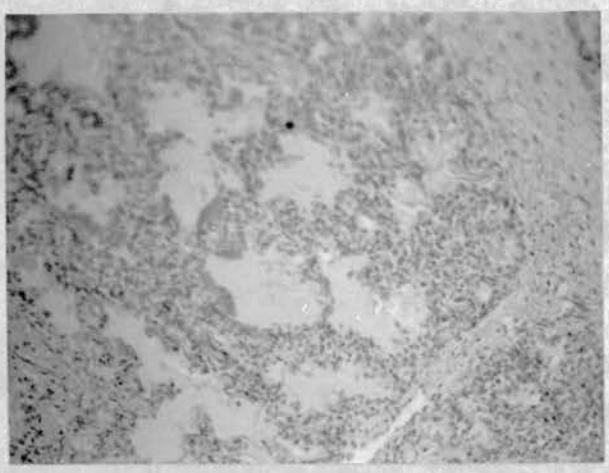

Fig 67 (171) Lung x 250
Early hyaline membrane

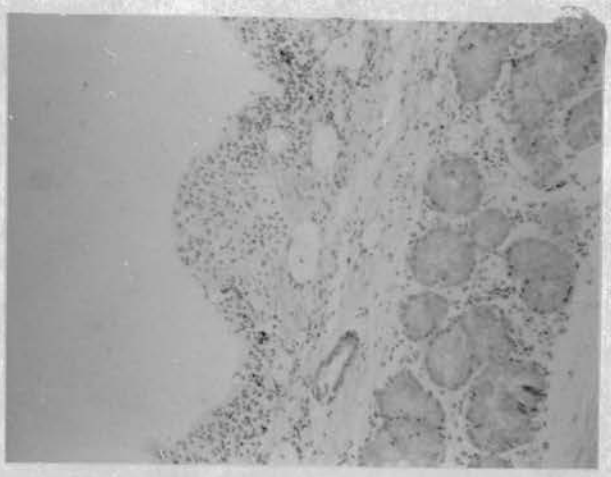

Fig 68 (171) Lung x 250
Desquamated bronchus
Infiltration

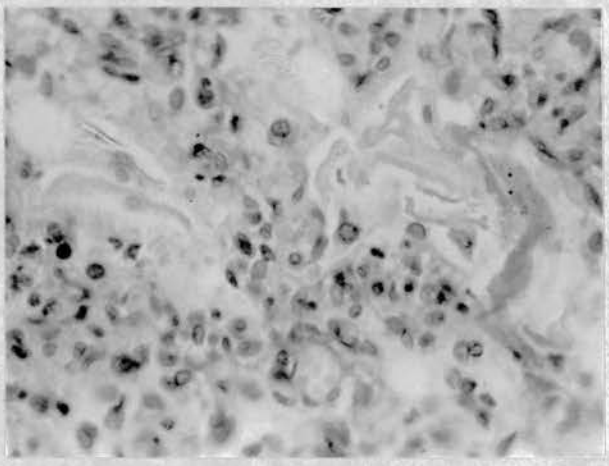

Fig 69 (171) Lung x 1000
Polymorphs

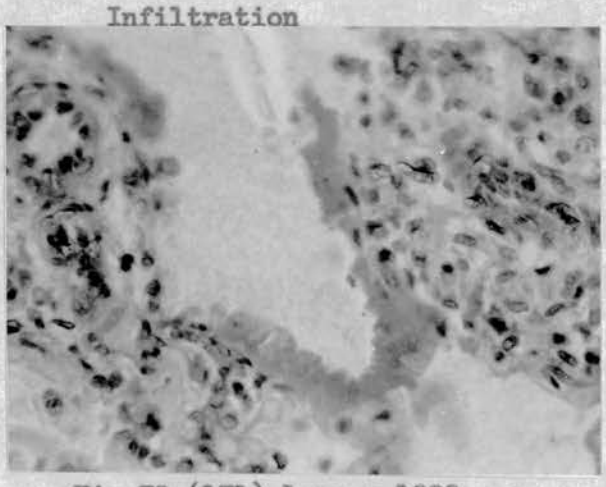

Fig 70 (171) Lung x 1000
Hyaline membrane

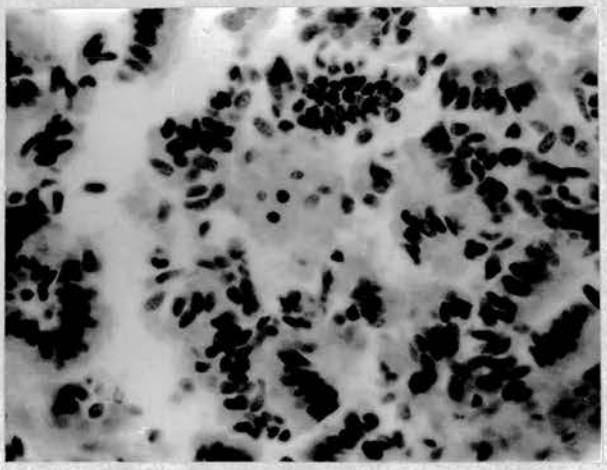

Fig 71 (33) Lung x 1000
Desquamated bronchus

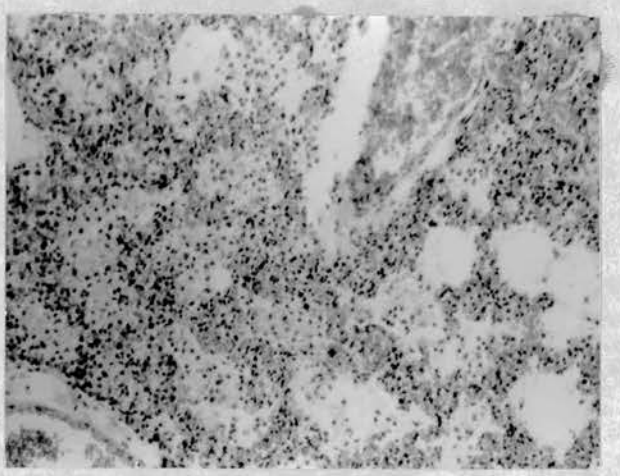

Fig 72 (33) Lung x 250
Mononuclear pneumonia

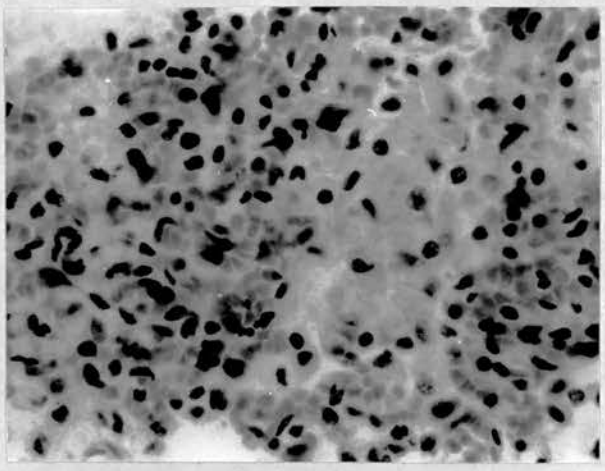

Fig 73 (33) Lung x 1000
Mononuclears and polymorphs

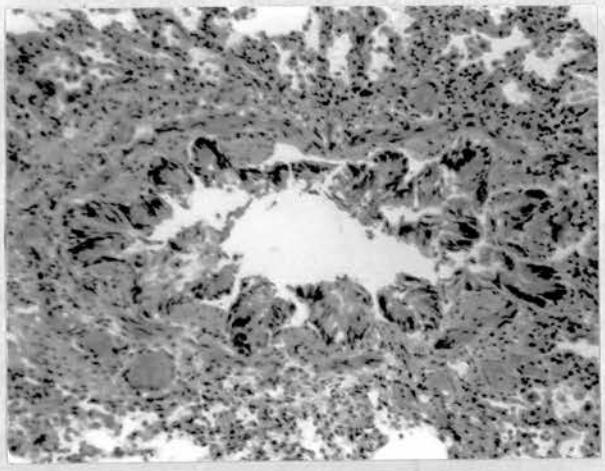

Fig 74 (127) Lung x 250
Bronchial desquamation

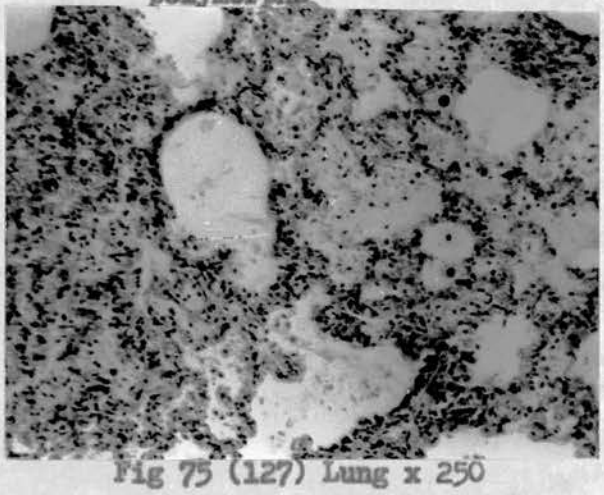

Fig 75 (127) Lung x 250
Mononuclear pneumonia

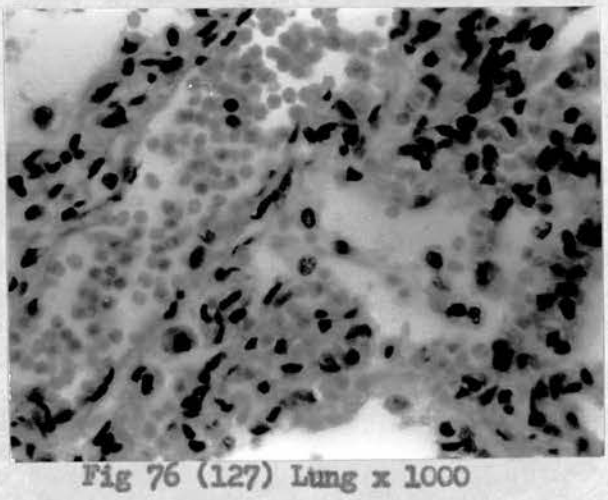

Fig 76 (127) Lung x 1000
Mononuclear pneumonia

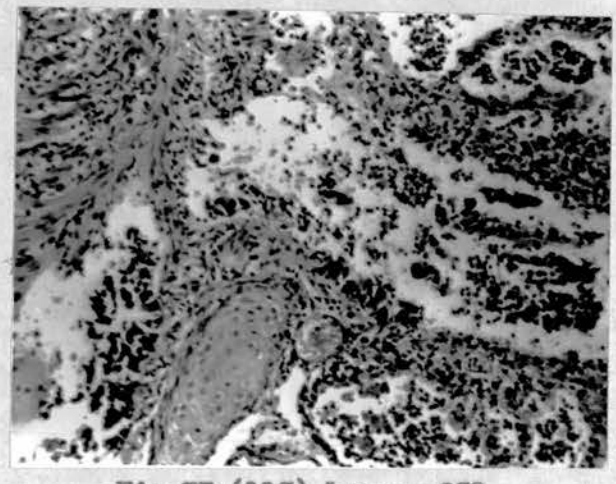

Fig 77 (115) Lung x 250
Disrupted bronchus

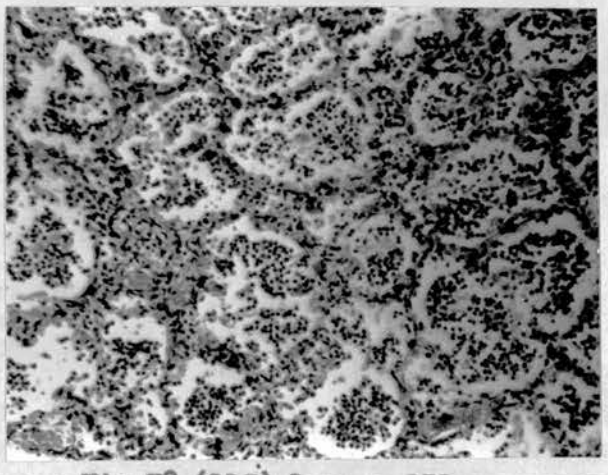

Fig 78 (115) Lung x 250
Consolidation

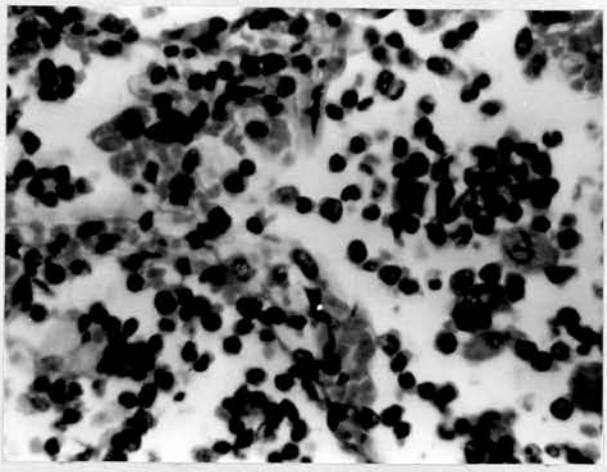

Fig 79 (115) Lung x 1000
Polymorphs and mononuclears

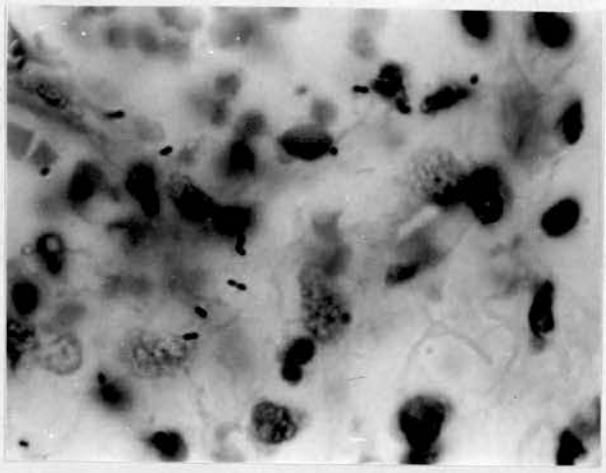

Fig 80 (113) Lung x 2500
Diplococci

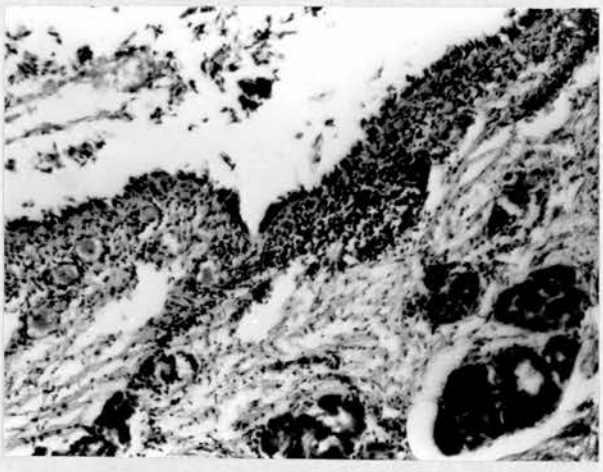

Fig 81 (203) Trachea x 250
Congestion and infiltration

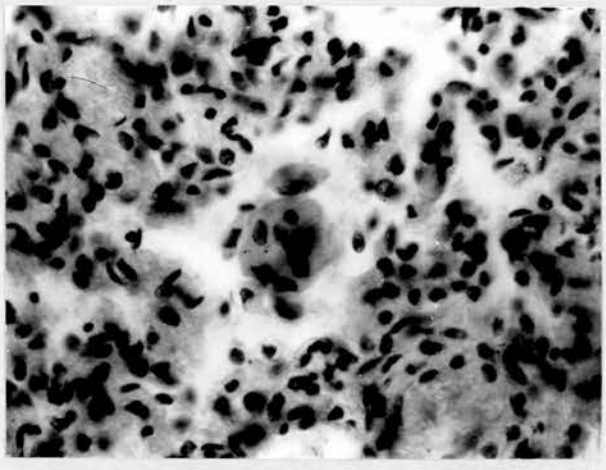

Fig 82 (203) Lung x 1000
Giant cells

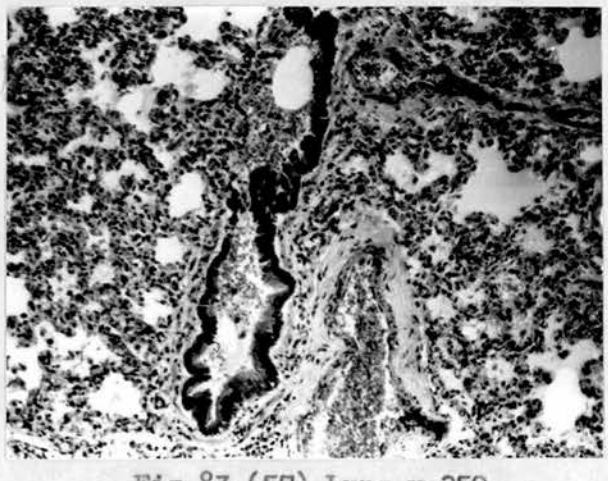

Fig 83 (57) Lung x 250
Disrupted bronchus

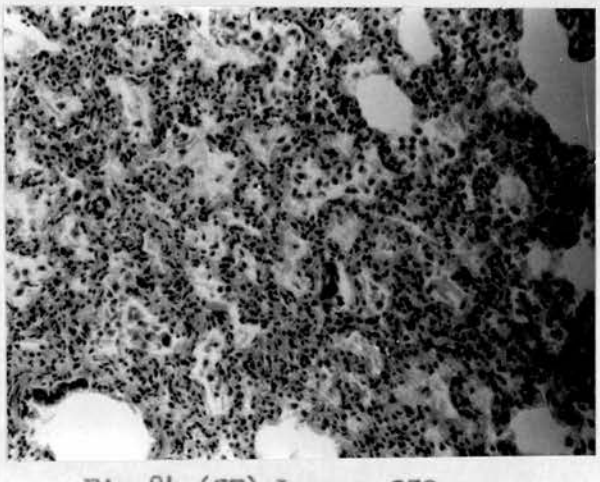

Fig 84 (57) Lung x 250
Mononuclear pneumonia

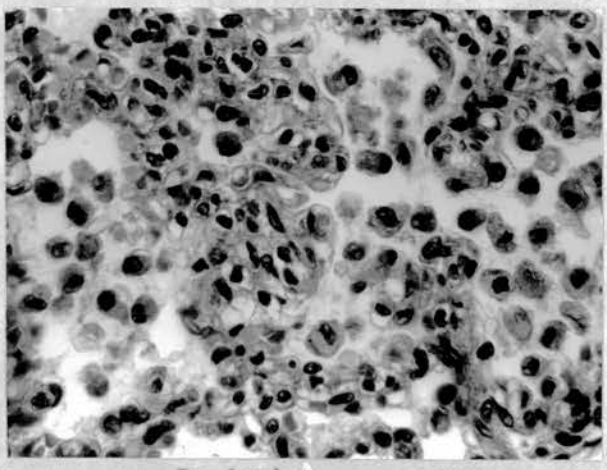

Fig 85 (57) Lung x 1000

Mononuclear pneumonia

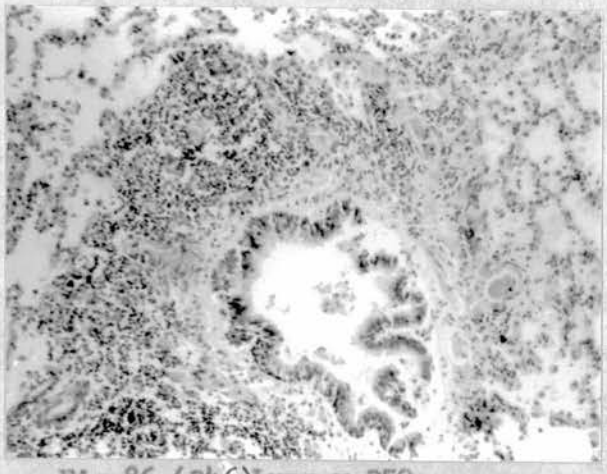

Fig 86 (246)Lung x 250

Broncho-pneumonia

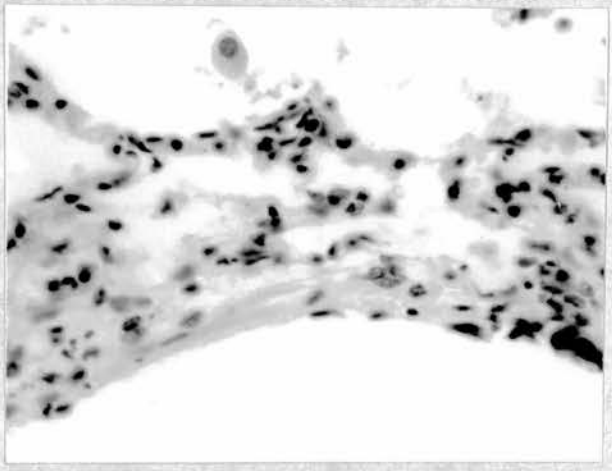

Fig 87 (246) Lung x 1000

Denudation of bronchus

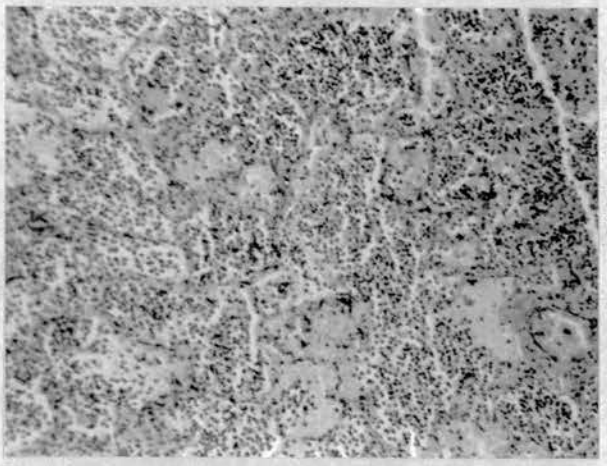

Fig 88 (16) Lung x 100

Broncho-pneumonia

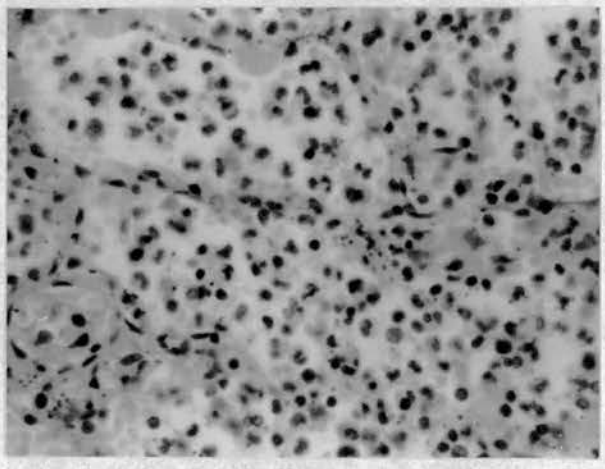

Fig 89 (16) Lung x 1000

Broncho-pneumonia

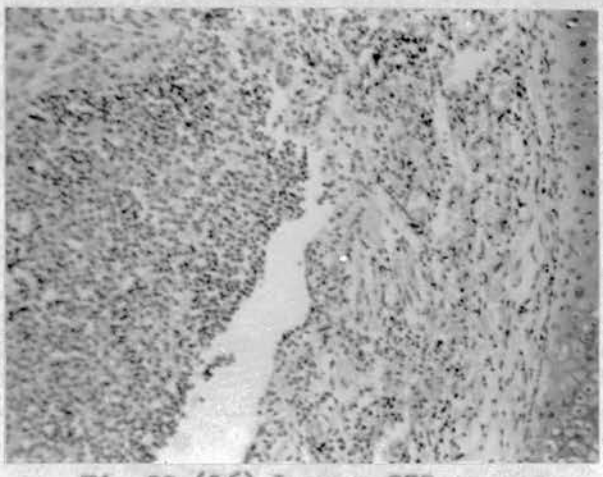

Fig 90 (16) Lung x 250

Micro-abscess

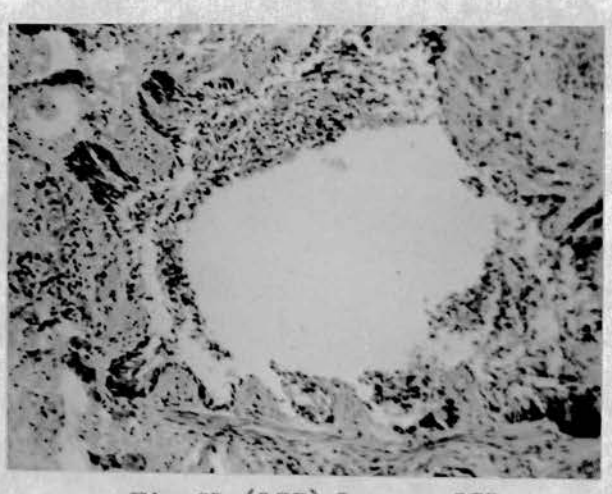

Fig 91 (153) Lung x 250
Desquamated bronchus

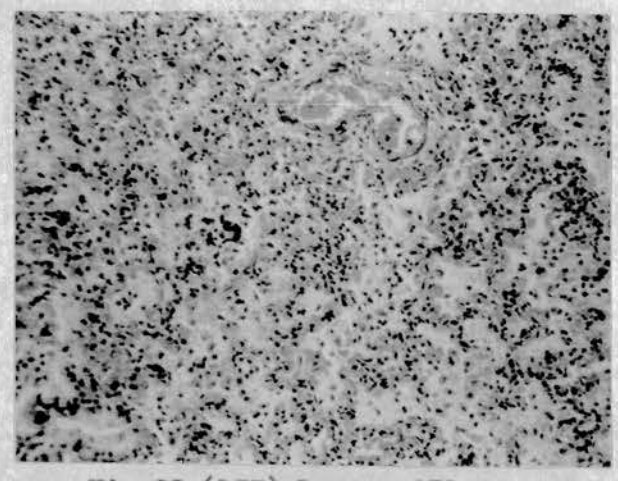

Fig 92 (153) Lung x 250
Mononuclear pneumonia

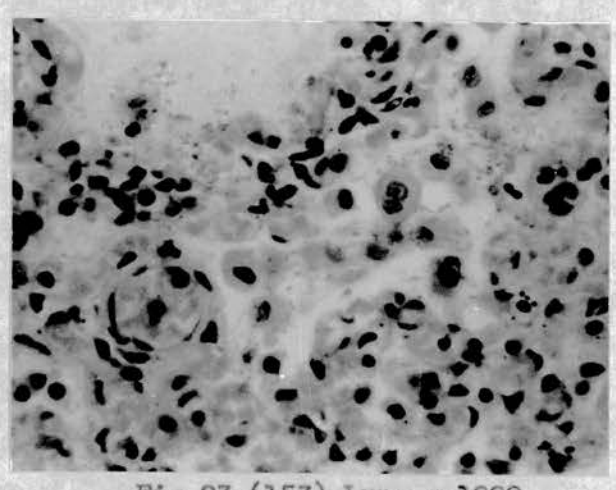

Fig 93 (153) Lung x 1000
Mononuclear pneumonia

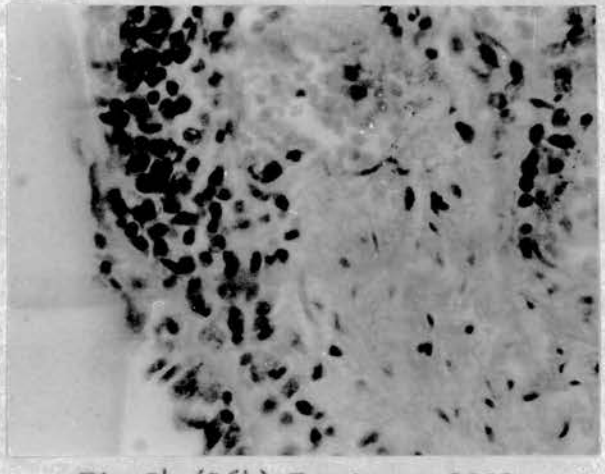

Fig 94 (164) Trachea x 1000
Denudation and infiltration

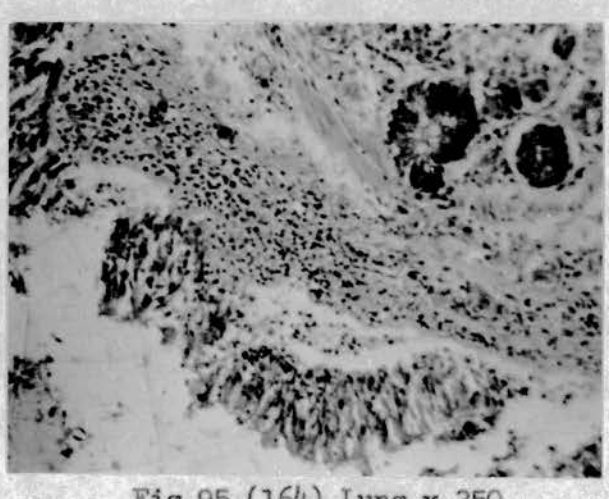

Fig 95 (164) Lung x 250
Desquamated bronchus
Infiltration

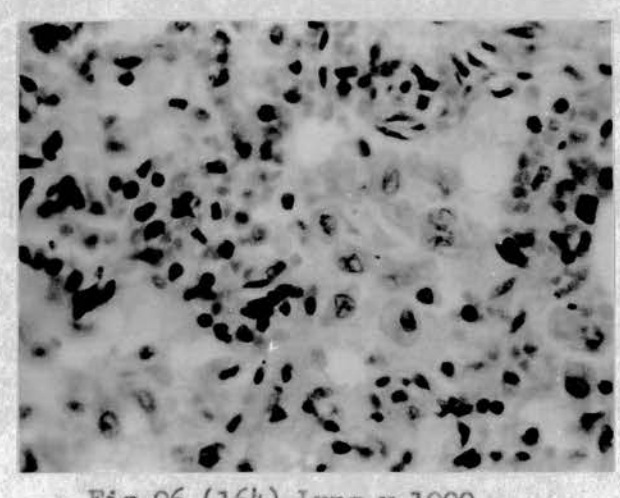

Fig 96 (164) Lung x 1000
Mononuclear pneumonia

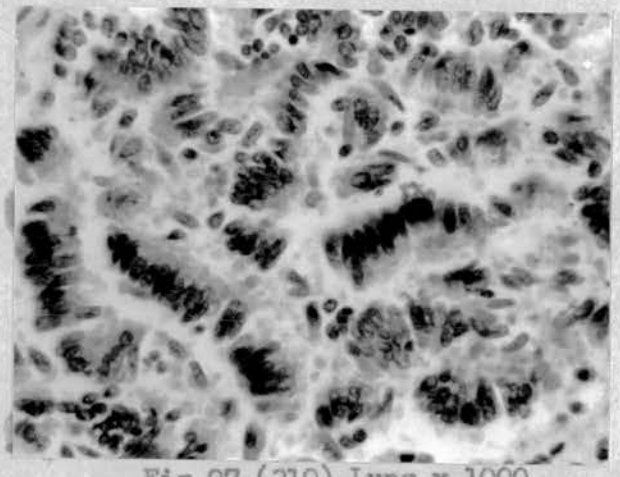

Fig 97 (210) Lung x 1000

Desquamated bronchus

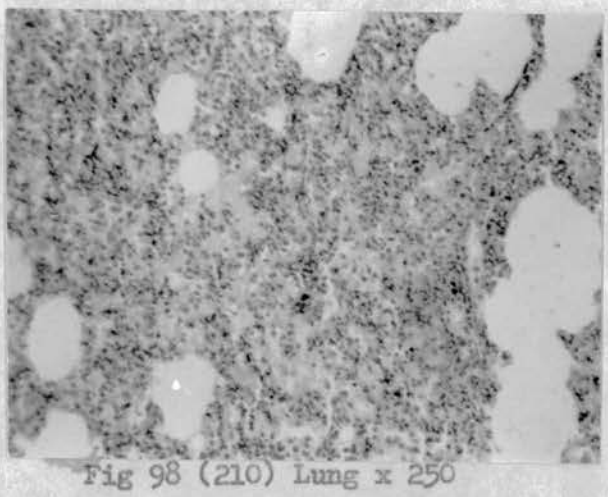

Fig 98 (210) Lung x 250

Consolidation

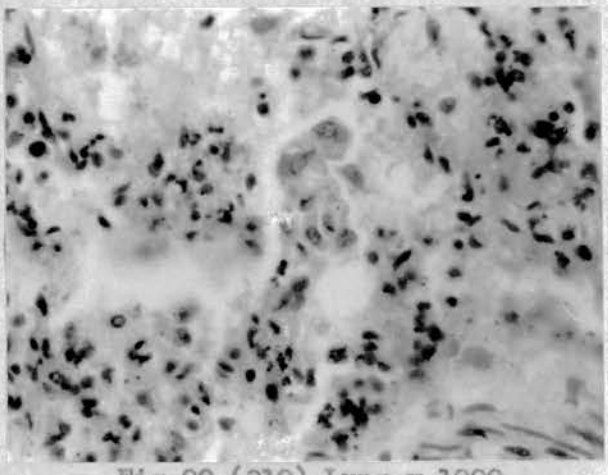

Fig 99 (210) Lung x 1000

Mononuclears and polymorphs

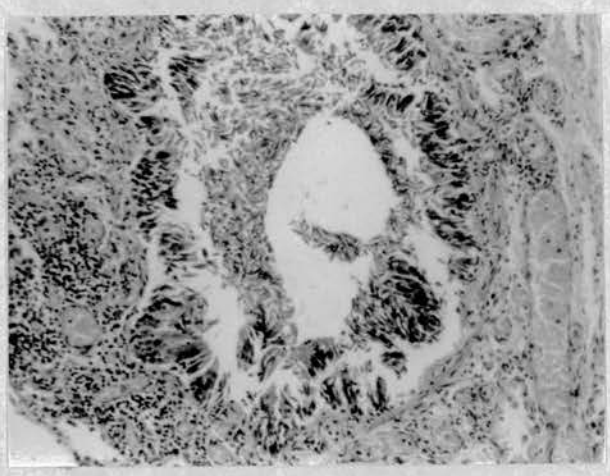

Fig 100 (252) Lung x 250

Disrupted bronchus

Infiltration

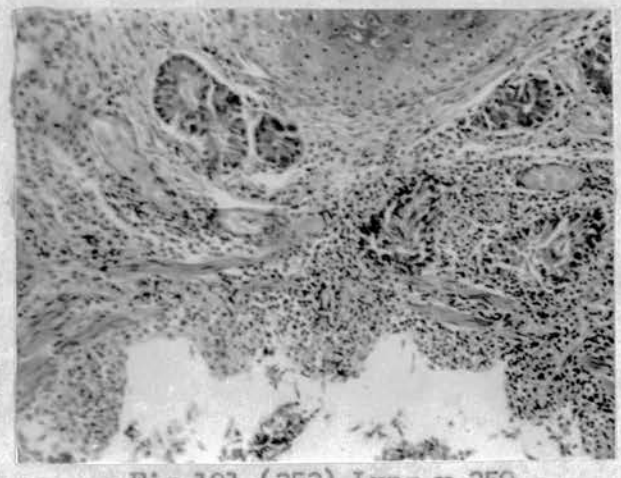

Fig 101 (252) Lung x 250

Disrupted bronchus

Infiltration

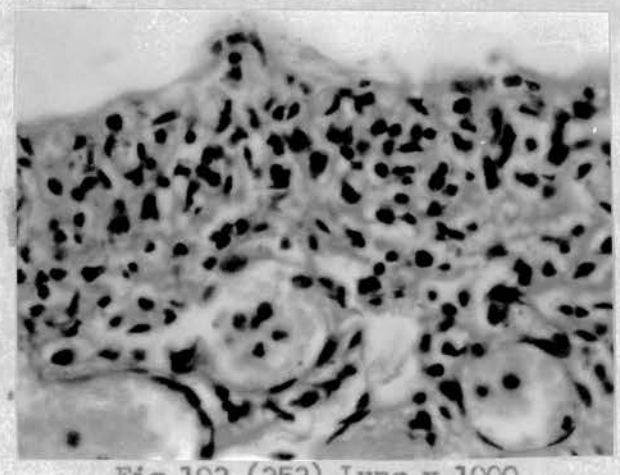

Fig 102 (252) Lung x 1000

Disrupted bronchus

Infiltration

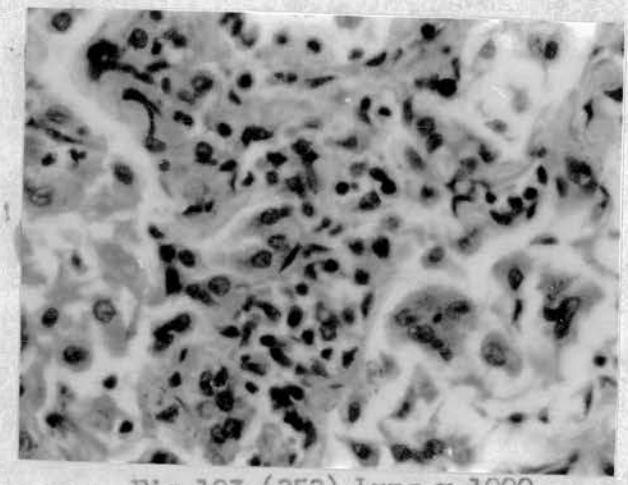

Fig 103 (252) Lung x 1000

Mononuclear and giant cells

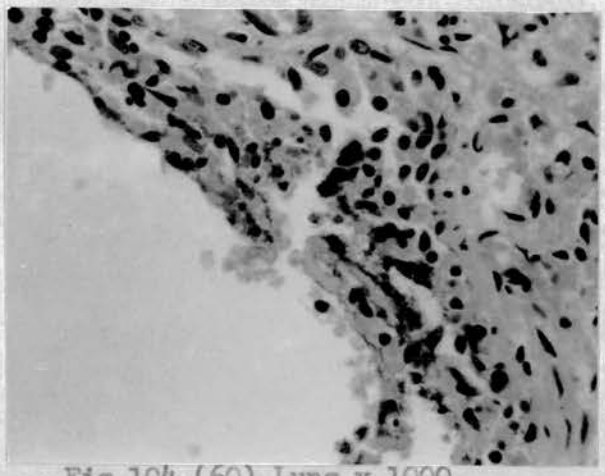

Fig 104 (60) Lung x 1000

Desquamated bronchus

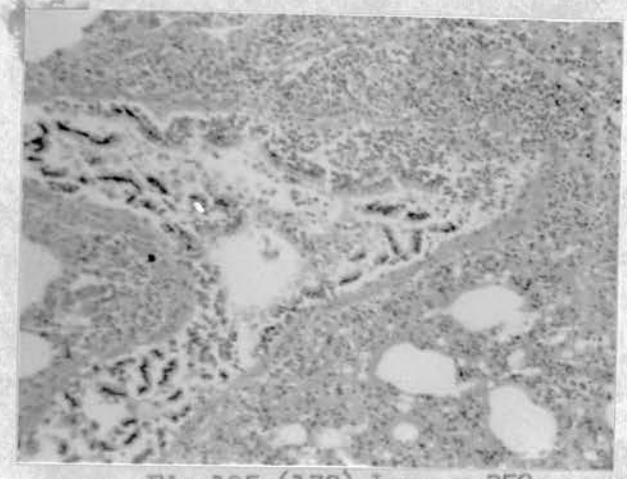

Fig 105 (132) Lung x 250

Disrupted bronchus

Infiltration

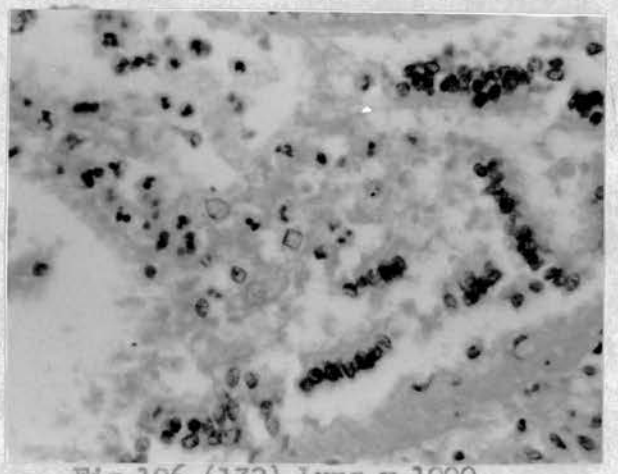

Fig 106 (132) Lung x 1000

Desquamated bronchus

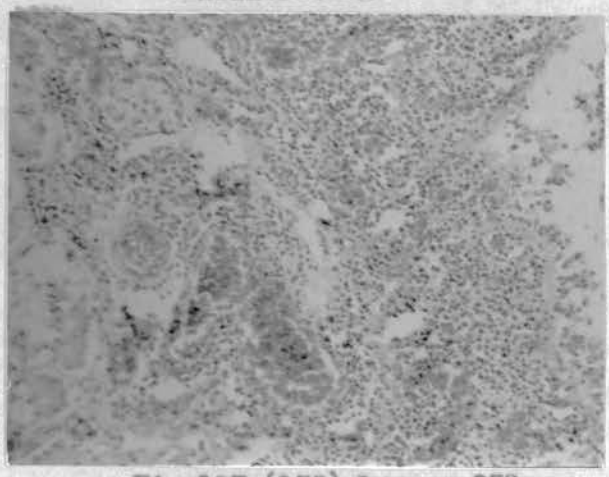

Fig 107 (132) Lung x 250

Broncho-pneumonia

Fig 108 (114) Lung x 250

Broncho-pneumonia

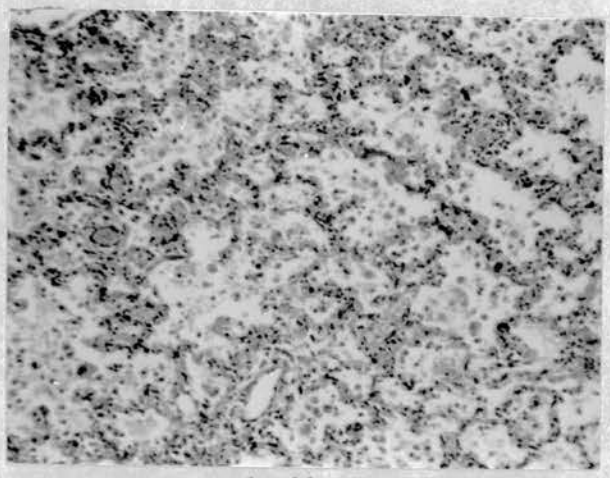

Fig 109 (114) Lung x 250

Mononuclear pneumonia

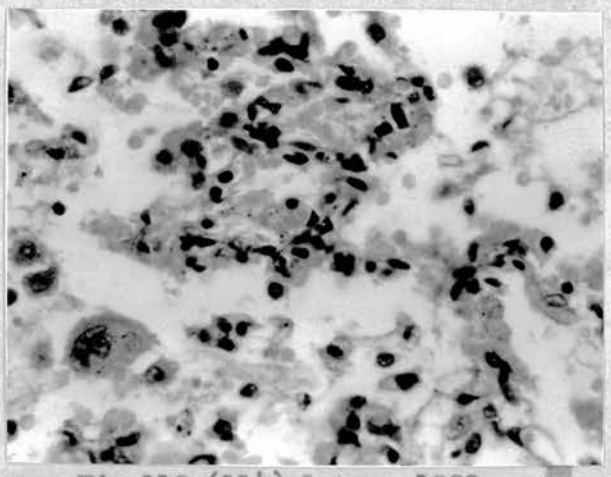

Fig 110 (114) Lung x 1000

Mononuclear and giant cells

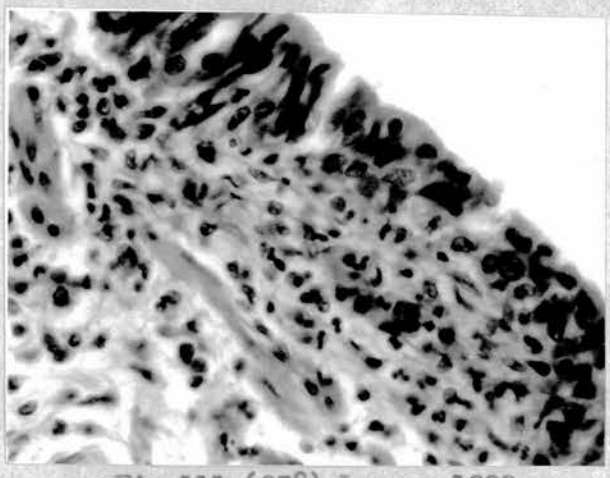

Fig 111 (238) Lung x 1000

Bronchial infiltration

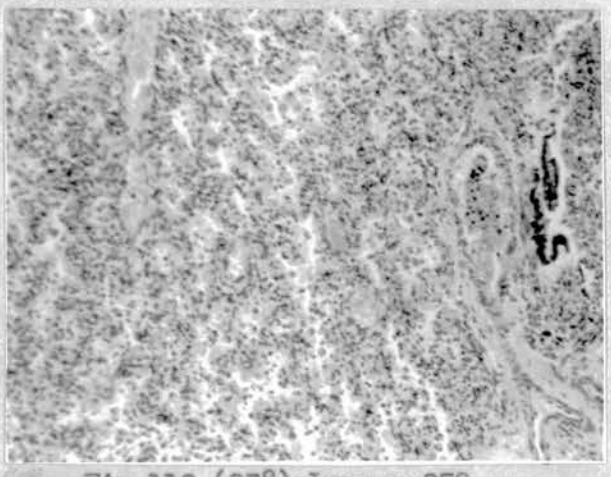

Fig 112 (238) Lung x 250

Mononuclear pneumonia

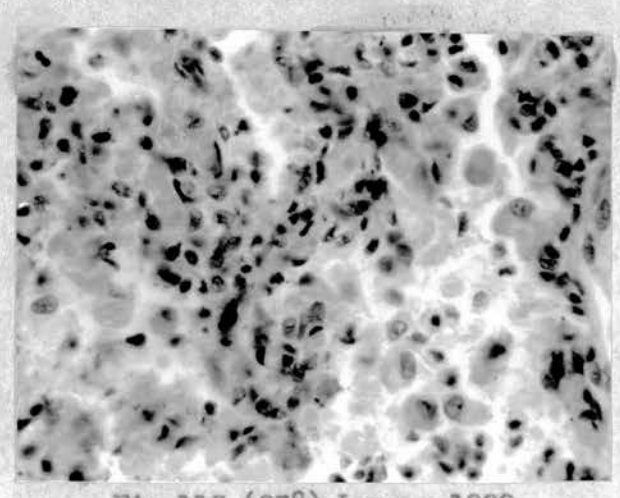

Fig 113 (238) Lung x 1000

Mononuclear pneumonia

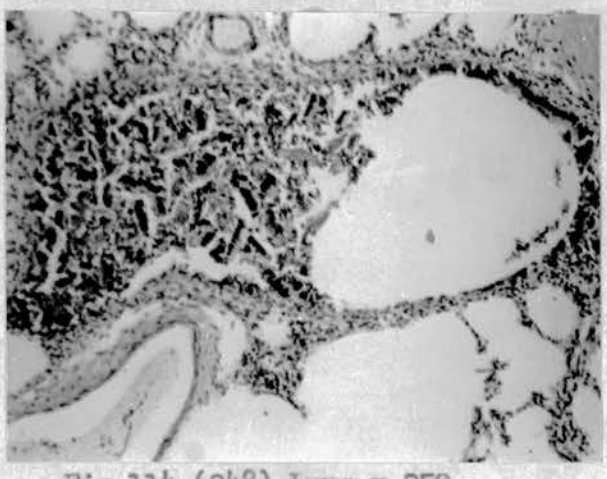

Fig 114 (248) Lung x 250

Desquamated bronchus

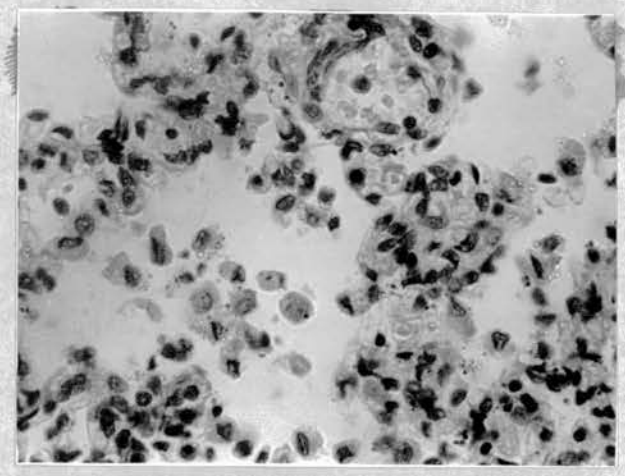

Fig 115 (248) Lung x 1000
Interstitial pneumonia

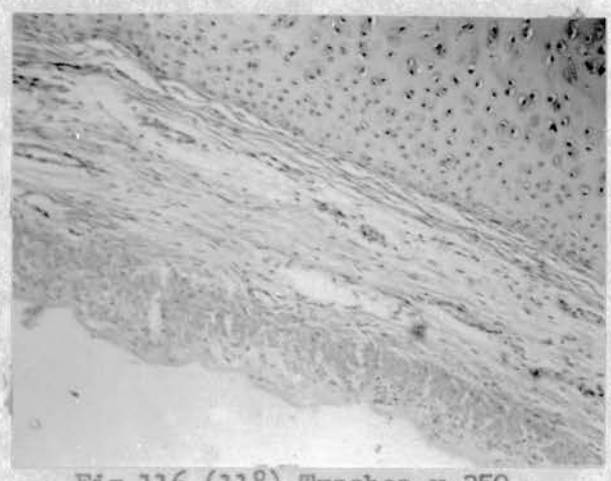

Fig 116 (118) Trachea x 250
Desquamation

Fig 117 (118) Lung x 250
Haemorrhage

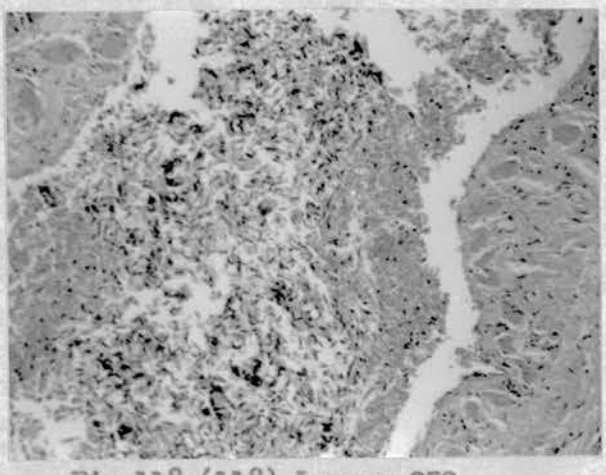

Fig 118 (118) Lung x 250
Disrupted bronchus

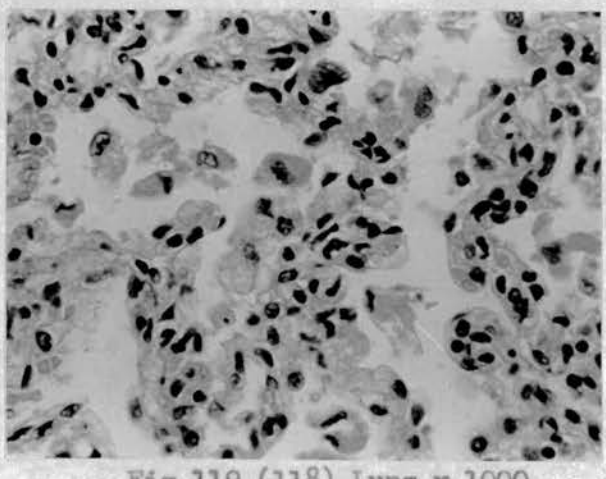

Fig 119 (118) Lung x 1000
Mononuclears

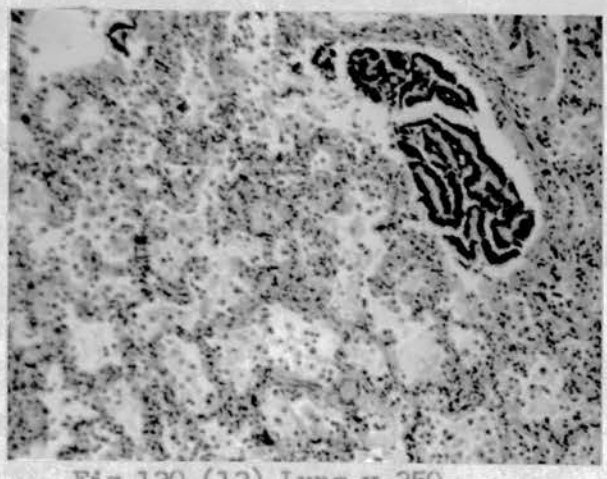

Fig 120 (12) Lung x 250
Desquamated bronchus
Mononuclear pneumonia

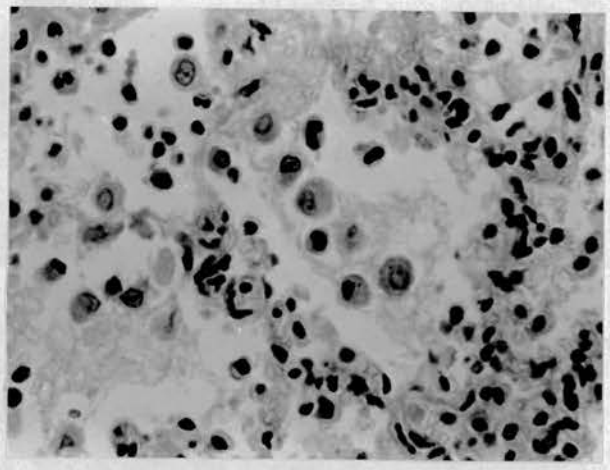

Fig 121 (12) Lung x 1000

Mononuclears and polymorphs

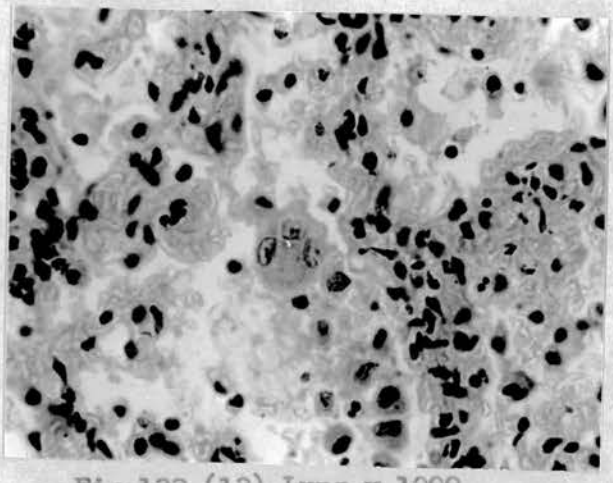

Fig 122 (12) Lung x 1000

Giant cells

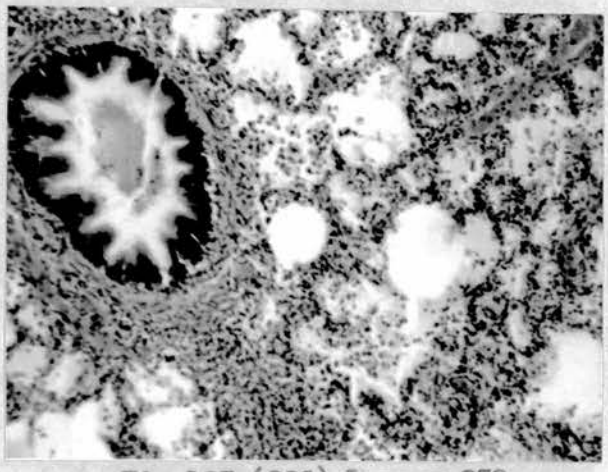

Fig 123 (229) Lung x 250

Mononuclear pneumonia

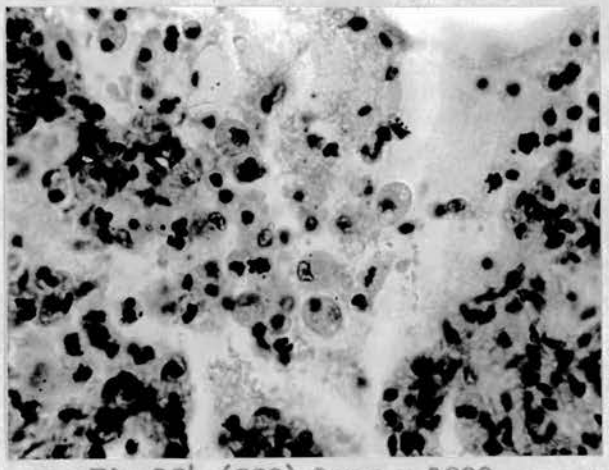

Fig 124 (229) Lung x 1000

Mononuclear pneumonia

Some polymorphs

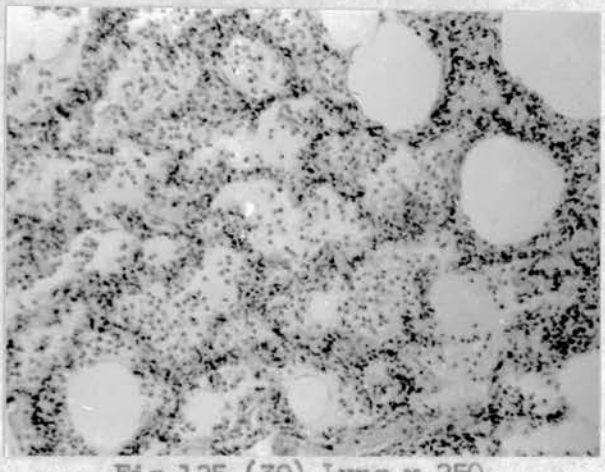

Fig 125 (39) Lung x 250

Mononuclear pneumonia

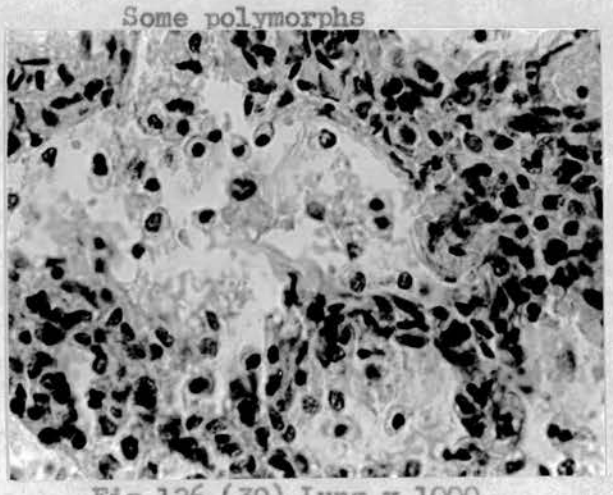

Fig 126 (39) Lung x 1000

Interstitial and

mononuclear pneumonia

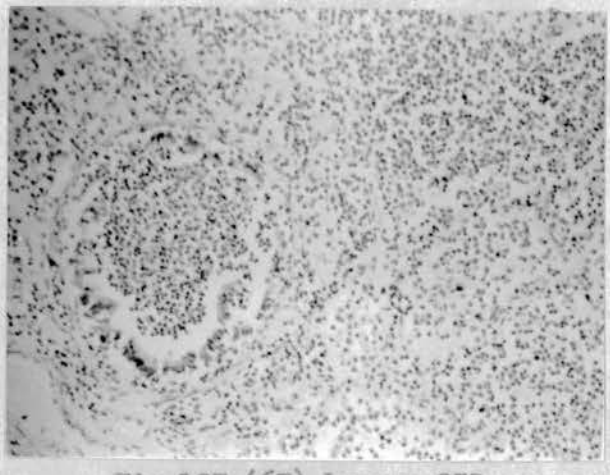

Fig 127 (67) Lung x 250

Broncho-pneumonia

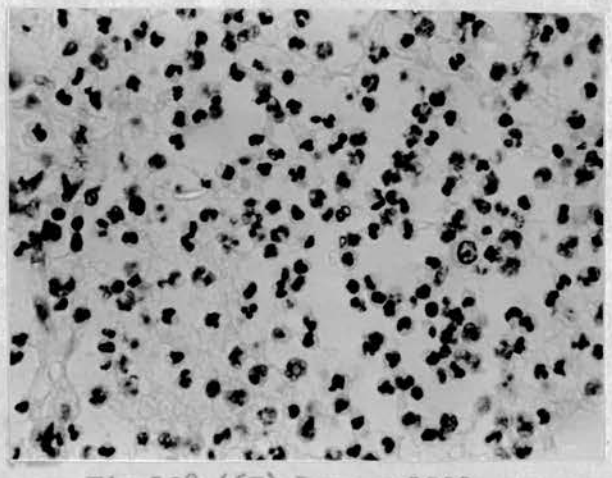

Fig 128 (67) Lung x 1000

Polymorph infiltration

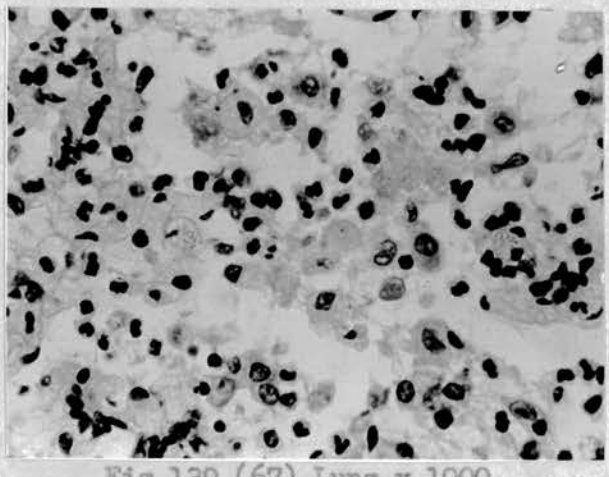

Fig 129 (67) Lung x 1000

Mononuclears

Some polymorphs

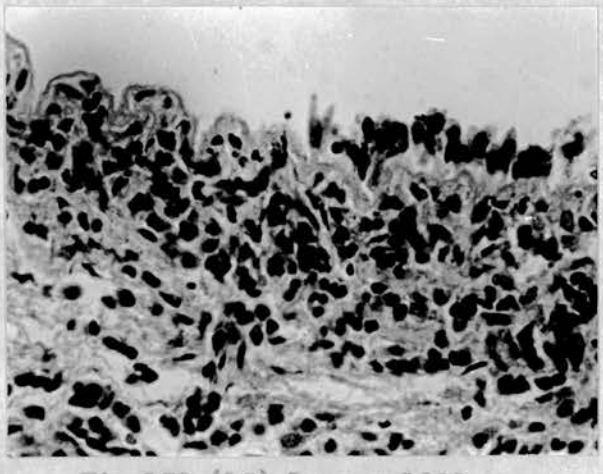

Fig 130 (19) Lung x 1000

Desquamated bronchus

Infiltration

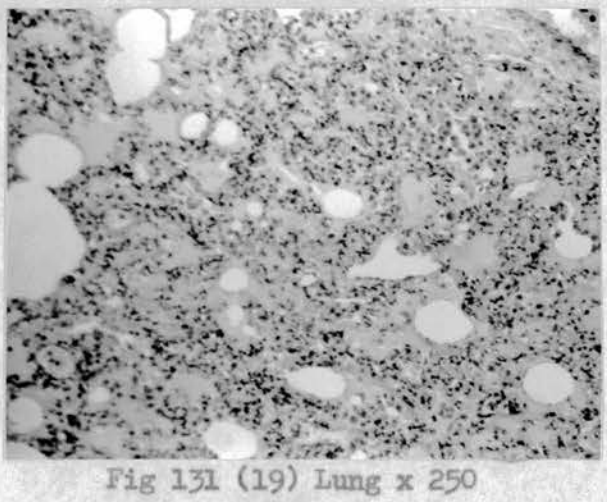

Fig 131 (19) Lung x 250

Mononuclear pneumonia

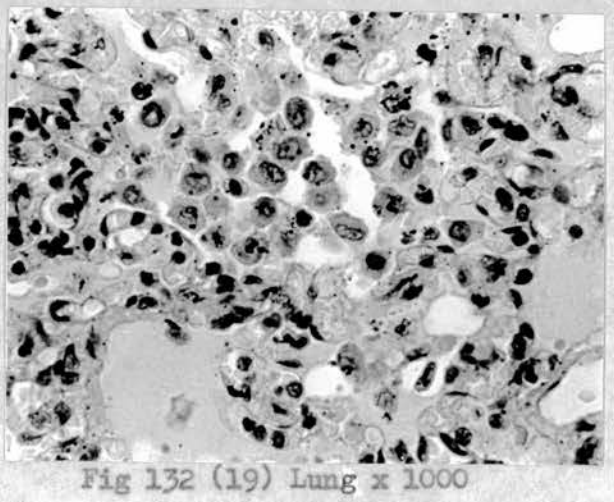

Fig 132 (19) Lung x 1000

Mononuclear pneumonia

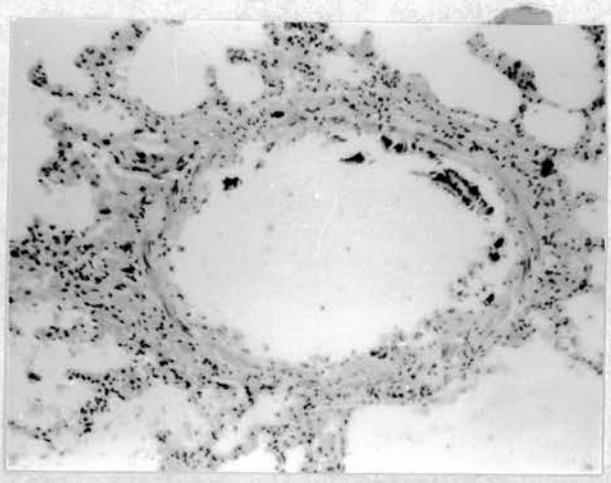

Fig 133 (5) Lung x 250
Denuded bronchus

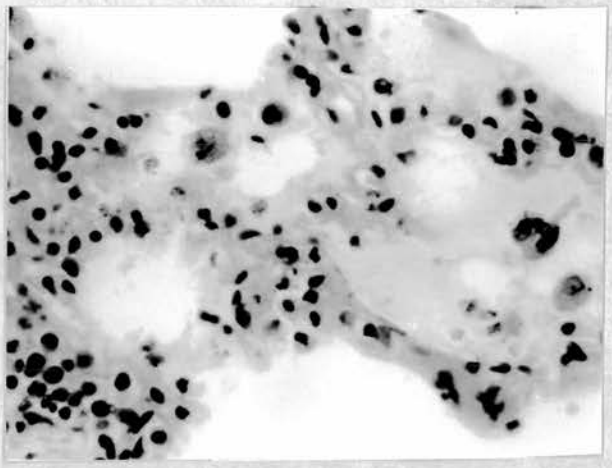

Fig 134 (5) Lung x 1000
Interstitial pneumonia

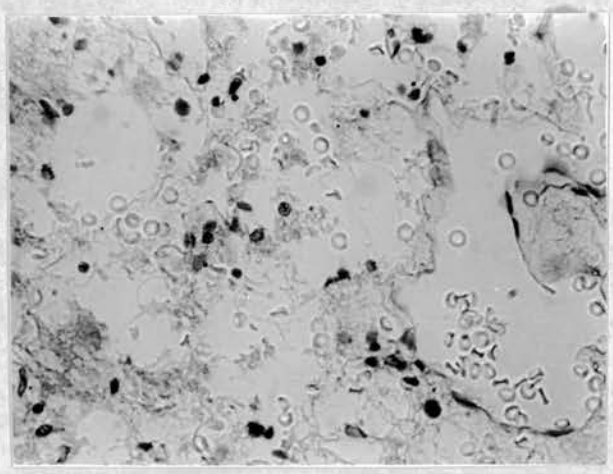

Fig 135 (213) Brain x 1000
Inflammatory cells in meninges

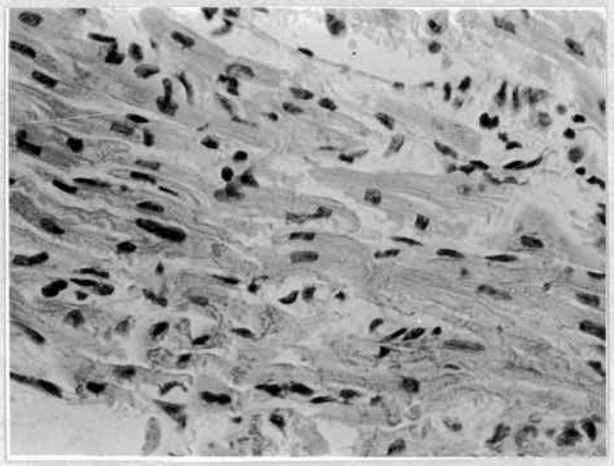

Fig 136 (213) Heart x 1000
Occasional inflammatory cells

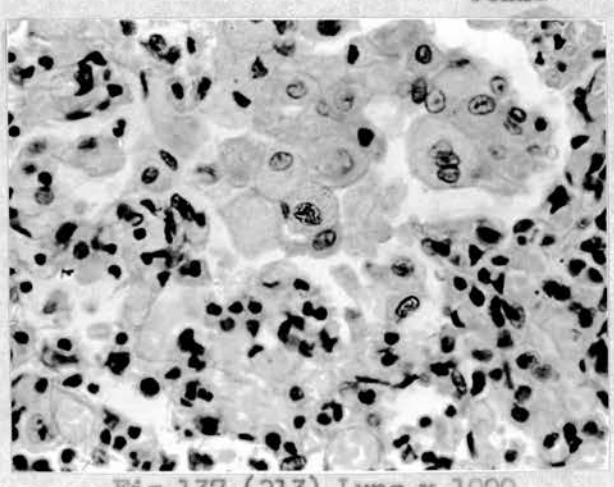

Fig 137 (213) Lung x 1000
Mononuclear pneumonia
Some polymorphs

APPENDIX E

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